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THE UNIVERSITY OF ALBERTA

THE CHEMISTRY OF ISOPRENE-$Fe(CO)_3$ ANION

by

CHRISTOPHER INGO FINCHAM

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF MASTER OF SCIENCE

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

FALL 1987

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submitted by CHRISTOPHER INGO FINCHAM

in partial fulfilment of the requirements for the degree of MASTER OF SCIENCE.

Supervisor

DATE 5th October 1987.

"To my parents"

ABSTRACT

A study was undertaken to investigate the feasibility of using isoprene iron tricarbonyl as a masked form of isoprene. In this investigation it was shown that the complex could be deprotonated at -78°C by the use of the base lithium 2,2,6,6-tetramethylpiperidide in conjunction with hexamethylphosphoramide (HMPA). The resulting anion was shown to react with a variety of electrophiles to produce new iron tricarbonyl complexes. Treatment of these complexes with either ceric ammonium nitrate or trimethylamine N-oxide as oxidants, resulted in decomplexation to produce the corresponding isoprene derivatives.

Finally, it was also discovered that the isoprene iron tricarbonyl anion undergoes an isomerisation on warming from -78°C to room temperature to give, after hydrolysis, the isomeric and structurally interesting complex (methyltrimethylenemethane)iron tricarbonyl.

ACKNOWLEDGEMENTS

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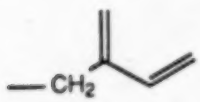
INTRODUCTION

The isoprene unit 1 is an important constituent of a number of natural products including examples such as the sesquiterpene aldehyde β-sinesal 2 (isolated from the Chinese orange, Citrus sinensus L. by Stevens and coworkers,[1] and subsequently synthesised by a number of groups[2]),



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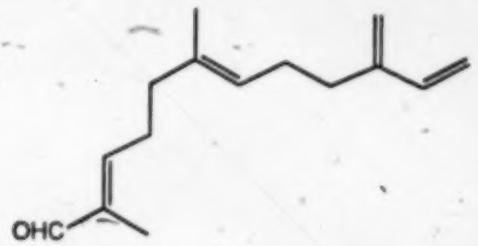
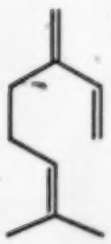


2

myrcene 3, a monoterpene found in a variety of plants,[3] and the terpene alcohols 2-methyl-6-methylene-7-octen-4-ol, 4, and 2-methyl-6-methylene-2,7-octadien-4-ol, 5, two of the major components of the sex attractant/aggregation pheromone of the male bark bettle, Ips Confusus.[4]



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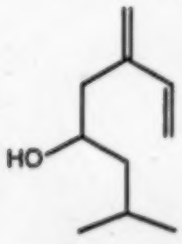

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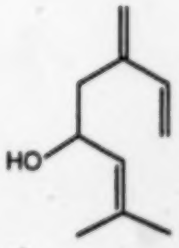

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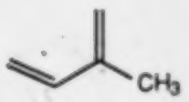
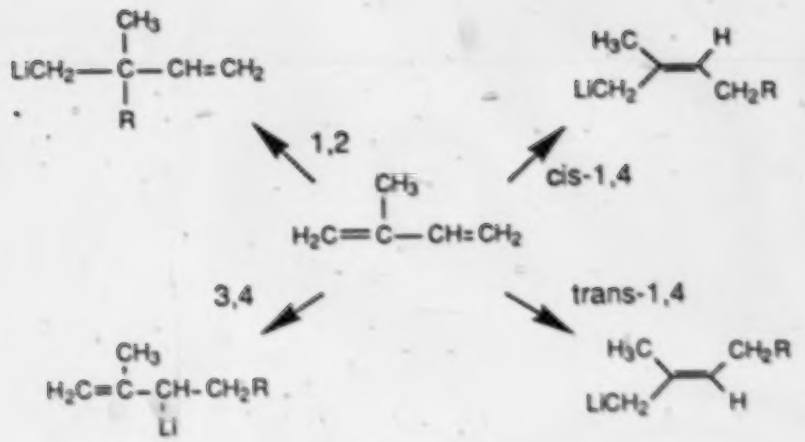
This makes the functionalisation of isoprene, 6, via deprotonation of the methyl group and reaction with electrophiles a worthwhile synthetic target.



6

The synthetic problem is made more challenging by the fact that the normal reaction of isoprene with various organolithium compounds does not result in deprotonation but rather in polymerisation, which arises from the lithium reagent acting as a nucleophile rather than a base. Nucleophilic addition to the diene produces a new organolithium species, which in turn can add to a second molecule of diene, ultimately leading to oligomerisation. The modes of addition of organolithium compounds (RLi) to isoprene are given in Scheme I.[5]

Much work has been done on these modes of addition in an attempt to find the conditions necessary to bring about repeated cis-1,4-addition since the resulting cis-polymers have properties resembling those of natural rubber. The type of addition favoured appears to depend upon the organolithium used and the solvent. For example, the



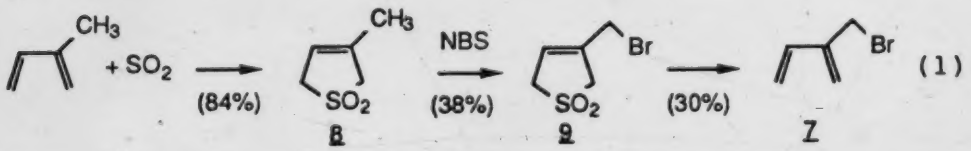
Scheme I

reaction of n-butyllithium with isoprene in cyclohexane produces mainly cis-1,4-addition, whereas changing the solvent to tetrahydrofuran results in products from the other three modes of addition, but no cis-1,4-addition.

A number of synthetic schemes have been devised to circumvent the polymerisation problems. In one approach[6] the isoprene moiety is formed in a stepwise fashion via a Wittig reaction on a suitably substituted aldehyde or ketone, whereas in others, techniques have been developed for the intact incorporation of the isoprene unit. The latter will be discussed in more detail below. Others still,[7] particularly in regard to the chiral synthesis of 4 and 5, have used totally different approaches although

these tend not to be of general synthetic use as a method to incorporate the diene unit.

In 1968 Silverstein and coworkers[8] published details of the synthesis of the terpene alcohols 4 and 5 which they had isolated earlier.[4] Their attempts centred on the use of 2-bromomethylbutadiene 7 as an isoprene synthetic equivalent. This compound, a common synthetic equivalent in a number of papers, was first synthesised by Krug and Yen[9] via 3-methyl-2,5-dihydro-thiophene-1,1-dioxide, 8 (formed from isoprene and sulphur dioxide[10]), reaction of the latter with N-bromosuccinimide (NBS), and pyrolysis of the resulting 3-bromomethyl-2,5-dihydrothiophene-1,1-dioxide, 9, to 7 (eq. 1).

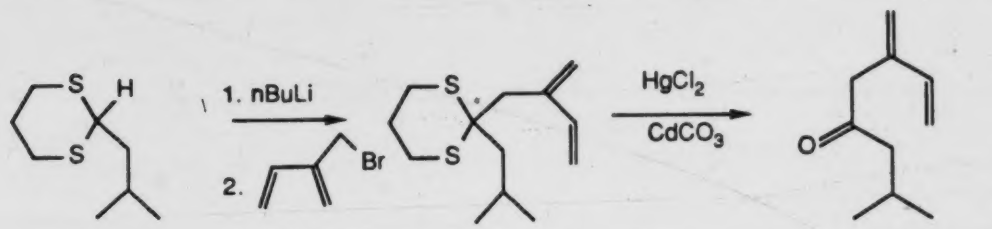


(1)

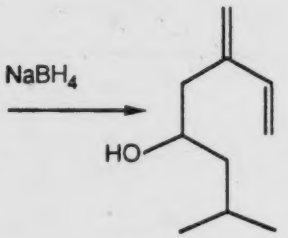
(Improved yields for the bromination (66%) and thermolysis (60-75%) have subsequently been reported.[11])

It was initially hoped that 7 could be converted into the organolithium or the Grignard reagent, and then reacted with isovaleraldehyde to produce 4. This was unsuccessful however, and no details are given of what products did result from the reaction of 7 with either

lithium or magnesium. As a result, the authors used **7** as the electrophilic component of the synthesis, and reacted it with the anion of 2-isobutyl-1,3-dithiane **10**, an activated form of isovaleraldehyde. This was followed by removal of the protecting group and reduction of the resulting ketone **11** to **4** as outlined in eq. 2.



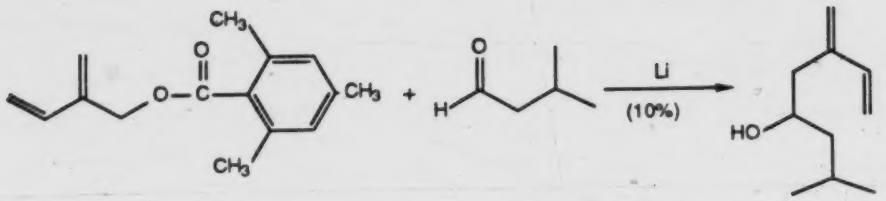
10 **11** (2)



4

The formation of an organometallic compound from **7**, and its use in the synthesis of **4**, was accomplished by Katzenellenbogen and Lenox,[12] using two procedures. The first involved the *in situ* generation of the organolithium intermediate via reaction of 2-(mesitoyloxymethyl)-1,3-butadiene **12** (prepared from the corresponding alcohol, in turn produced from **7**[13]) with lithium in tetrahydrofuran in the presence of isovaleraldehyde **13** to give **4** in 10% yield

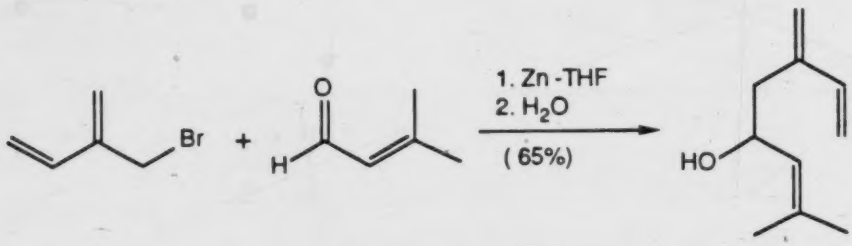
(eq. 3).



(3)

12 13 4

The second procedure used the in situ generation of an organozinc species in a "Reformatsky-type procedure", via reaction of 7 with zinc in tetrahydrofuran in the presence of 13 to produce 4 in 52% yield. This latter method was used in a collaborative study of Silverstein and Katzenellenbogen[14] to produce the other component of the pheromone, 5, via reaction of 7 with zinc and 3-methyl-2-butenal 14 (eq. 4).

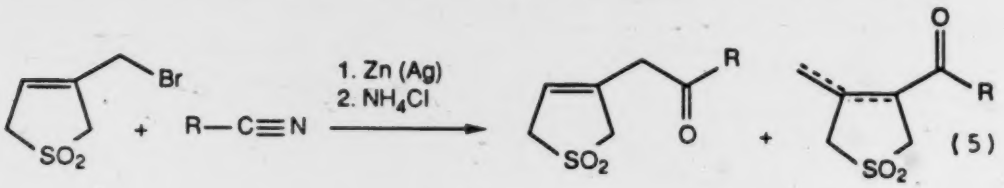


(4)

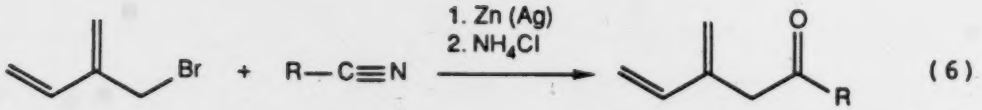
7 14 5

The reaction is also successful for the condensation of allylic bromides (of which 7 is a member) with organonitriles, and has been used by Rousseau and Drouin[15] to produce a variety of ketones containing the isoprene functionality, including the precursors to 4 and 5. The

reaction can be carried out either with the sulphur dioxide adduct of 2-bromomethyl-1,3-butadiene **9** (eq. 5), or with 2-bromomethyl-1,3-butadiene **7**, itself (eq. 6), although the former results in a mixture of products, of which the desired product is only the minor component.

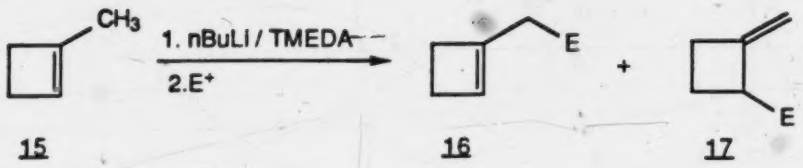


9 20-30% 80-70% (5)



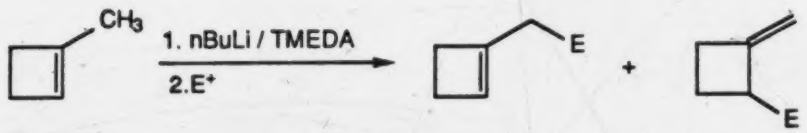
7 70-85% (6)

An alternative approach to the diene problem has been developed by Wilson and coworkers[16] utilising methylcyclobutene, **15**, as an isoprene synthetic equivalent. This molecule possesses the requisite number of carbon atoms, and cyclobutenes are known to undergo thermal ring opening to give 1,3-dienes. Methylcyclobutene **15** was deprotonated using n-butyllithium/tetramethylethylenediamine (TMEDA), and then reacted with a variety of electrophiles according to eq. 7.



15 16 17 (7)

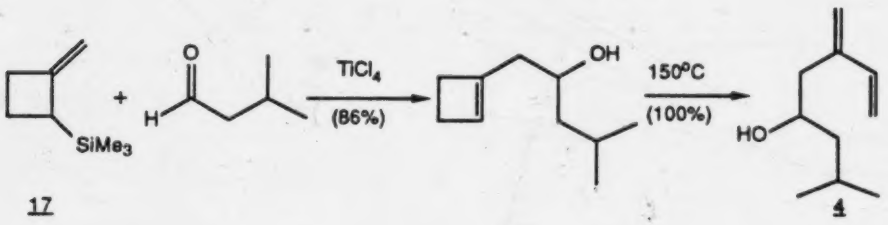
This method suffered from the drawback that two products were produced, and of these the undesired isomer **17**, tended to predominate. Although the reaction conditions (solvent and temperature) could be manipulated to favour formation of isomer **16**, the best ratio achieved was only about 2:1 and often this was done at the expense of the overall yield. A subsequent modification[17] to this procedure employed tin and silicon chemistry in which the electrophiles were chlorotrimethylstannane and chlorotrimethylsilane, respectively (eq. 8).



15 (8)

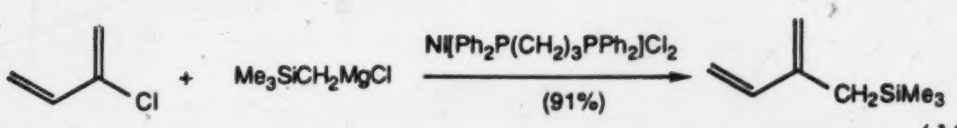
E= Me_3SnCl (85%)	80	20
E= Me_3SiCl (75%)	20	80

Compound **16** (E = $SiMe_3$) was separated from compound **17** (E = $SiMe_3$) by distillation at atmospheric pressure, and under these conditions the former underwent ring opening. In this way pure **17** (E = $SiMe_3$) was obtained, and utilised in subsequent Lewis acid ($TiCl_4$) catalysed reactions with electrophiles, including the preparation, after ring opening, of pheromone alcohol **4** (eq. 9).



17 **4** (9)

Another approach to this problem, utilising silicon chemistry, was reported by Sakurai and coworkers[18] who employed 2-trimethylsilylmethyl-1,3-butadiene **18** as an isoprene anion synthetic equivalent. This compound is formed via reaction of 2-chloro-1,3-butadiene (chloroprene) **19** with the Grignard reagent **20** formed from chloromethyltrimethylsilane under the influence of a nickel(II) catalyst (eq. 10).



19 **20** **18** (10)

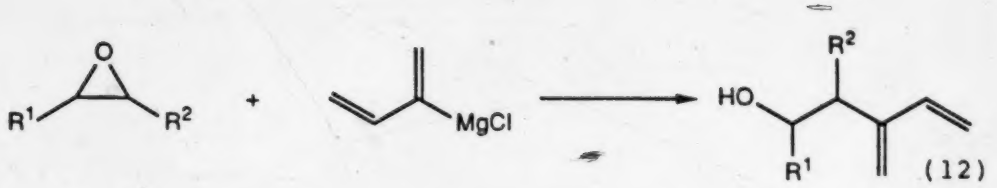
Compound **18** was reacted with acid chlorides, acetals, and aldehydes under Lewis acid ($TiCl_4$) catalysis to produce a series of isoprenylated products, including the pheromone alcohols **4** and **5**.

2-Chloro-1,3-butadiene **19** was also used as the starting material in another route[19] to the incorporation of the 1,3-diene moiety. From this compound was prepared the corresponding Grignard reagent, 2-(1,3-butadienyl)magnesium chloride **21**, which was reacted with a variety of ketones, aldehydes and epoxides. Reactions with the first two types of substrate resulted in a mixture of products (eq. 11), with the ratio being dependent on the steric

(11)

21 **22** **23**

size of the substrate (e.g. if R^1 and/or R^2 are bulky groups the allene product **23** is formed, while for most aldehydes (except R^1 = Ph), the product distribution is reversed). The reaction of **21** with epoxides gave the corresponding 1,3-dienyl alcohols in moderate to good yields (eq. 12).

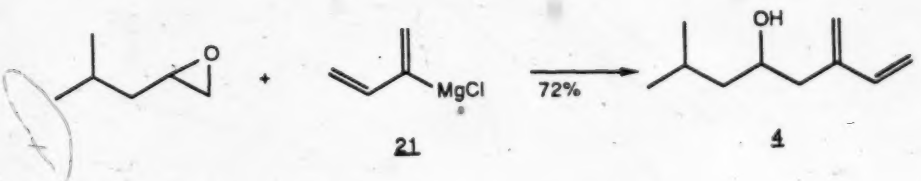


(12)

R^1=Et, R^2=H — 21 — 77%

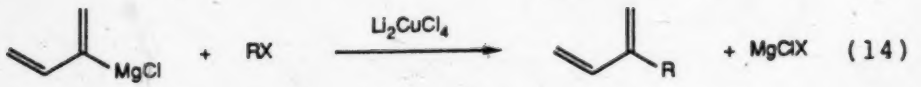
R^1=H, R^2=H — 50%

Although **21** is a butadiene anion synthon rather than an isoprene anion synthon, by suitable choice of electrophile similar products can be obtained from **21** as were obtained via the aforementioned synthon, as evidenced by the synthesis of pheromone **4** (eq. 13).



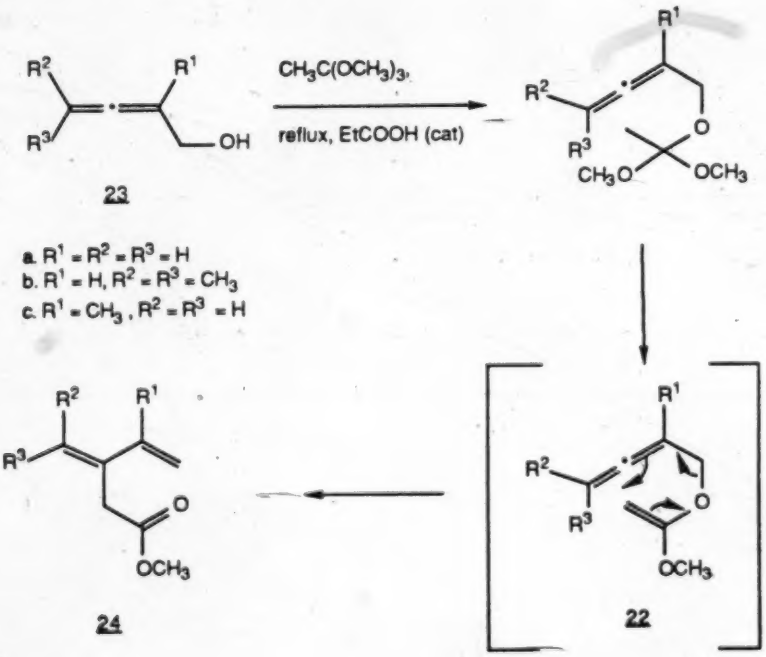
21 **4** (13)

The reaction of organometallic **21** with various alkyl, aryl, and vinyl halides under the catalysis of Li_2CuCl_4 (eq. 14), has also been shown by Nunomoto and coworkers[20] to result in butadiene derivatives (i.e. isoprene derivatives) in moderate to good yields.



21 (14)

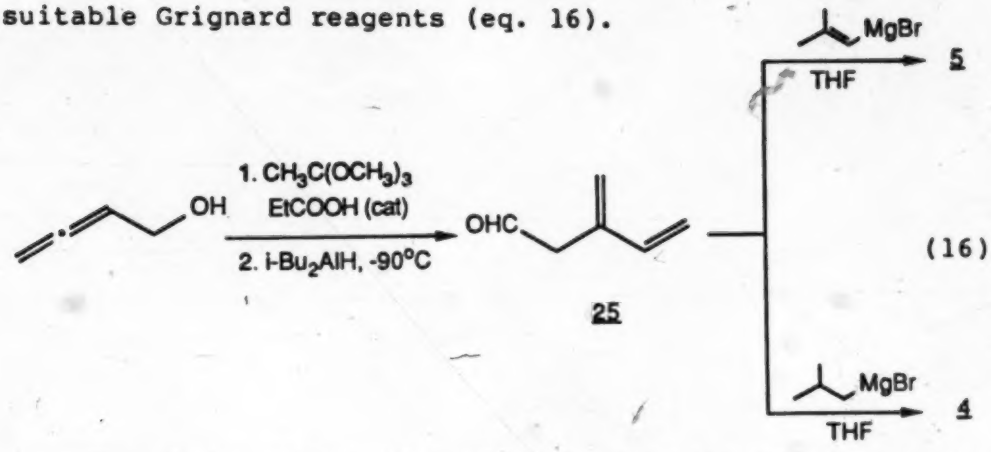
1,3-Dienyl compounds have also been prepared via the Claisen rearrangement of allenic ethers **22** produced by the reaction of allenic alcohols **23** with methyl orthoacetate as outlined in eq. 15.[21]



(15)

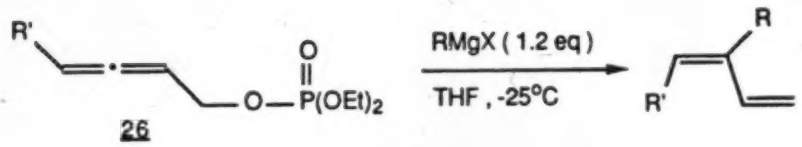
This method has been used to prepare the pheromone alcohols **4** and **5** by the reaction of aldehyde **25** (produced via diisobutylaluminum hydride reduction of **24a**) with

suitable Grignard reagents (eq. 16).



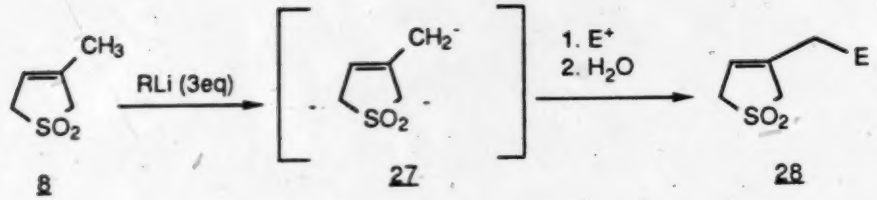
(16)

Phosphate esters of α-allenic alcohols **26** can also be used to prepare 1,3-dienes via reaction with Grignard reagents (eq. 17).[22]



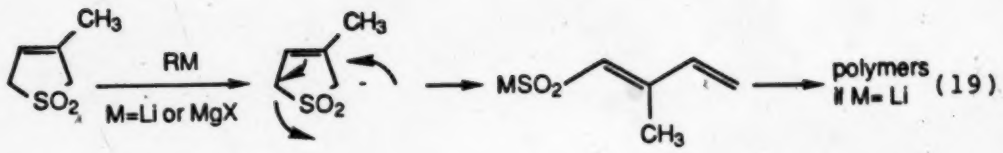
(17)

Our first approach to the "isoprene anion" problem centred upon the sulphur dioxide adduct of isoprene, 3-methyl-2,5-dihydrothiophene-1,1-dioxide, **8** (also known as 3-methyl-3-sulpholene), as a masked form of isoprene. The idea was to determine if the "trianion" **27** (or equivalent) could be formed and then reacted with various electrophiles (eq. 18).



8 27 28 (18)

It was hoped, by analogy with alkylation of the dianion of β-ketoesters,[23] that if the "trianion" was formed (trianions of polyketones have been formed[23a]), preferential attack of the electrophile should occur at the most basic position, resulting in compounds of the type indicated, **28**. The corresponding substituted isoprene derivative should then be available by thermal extrusion of sulphur dioxide. A number of organolithium bases were tried, including n-, sec- and t-butyllithium, methyllithium, and lithium tetramethylpiperidide (all with and without hexamethylphosphoramide), but none could be found to accomplish our goal. Instead, all attempts resulted in dark reaction mixtures, loss of the vinyl signal in the ^1H nmr (a phenomenon also noted by Ta-shue Chou and coworkers[24]), and polymerisation, possibly via the route indicated (eq. 19).



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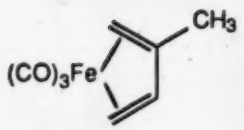
It should be noted that alkylation of the monoanion can be successfully achieved if the anion is generated in the presence of the alkylating agent.[24,25] Also, by use of a Grignard reagent in place of an organolithium compound, the ring opened product can be isolated as its magnesium salt **29** (M = MgBr).[26] Towards the end of this approach a paper appeared[27] in which the lifetime of the monoanion (generated using n-butyllithium/HMPA) was studied. It was reported that this anion was stable toward ring opening for up to 15 minutes when generated at -105°C, and could be successfully alkylated under these conditions. One final attempt was made to generate the "trianion" under these low temperature conditions but this again proved unsuccessful and this approach was then abandoned.

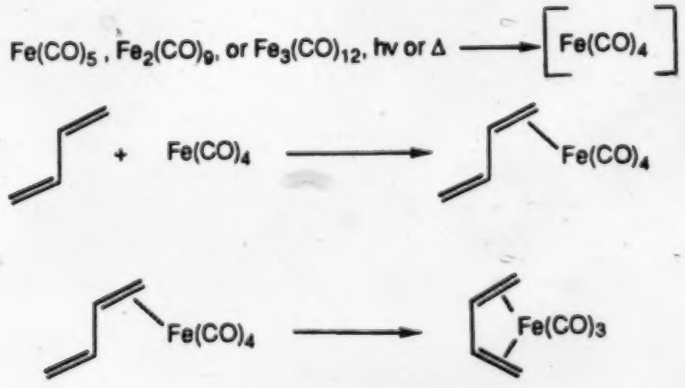
Our second approach to the problem centred on the use of tricarbonyl(2-methyl-1,3-butadiene)iron (commonly referred to as isoprene iron tricarbonyl) **30** as a masked

form of isoprene.



30

Complexes of this type are commonly formed via reaction of the diene with either iron pentacarbonyl ($Fe(CO)_5$), diiron nonacarbonyl ($Fe_2(CO)_9$) or triiron dodecacarbonyl ($Fe_3(CO)_{12}$). The reaction presumably involves the reactive intermediate species $Fe(CO)_4$ attacking one bond of the diene, with subsequent intramolecular attack by the other double bond and loss of carbon monoxide to form the η^4-coordinated species (Scheme II).



Scheme II

These compounds, while important in their own right, are of particular interest to organic chemists because of the profound effect that bonding to a metal atom has on the chemical properties of the organic segment. Some of these effects and their use in organic chemistry are described below as well as some methods that have been used to prepare these complexes.

The first acyclic diene iron tricarbonyl complex was prepared in 1930 by Reihlen and coworkers[28] via the high temperature reaction of butadiene and $Fe(CO)_5$ in a pressure vessel. $Fe(CO)_5$ is the least reactive of the common three iron carbonyl species, and a high (130-150°C) reaction temperature is necessary (presumably to generate the required $Fe(CO)_4$). Reihlen and coworkers also investigated the reaction of isoprene with $Fe(CO)_5$ under the same conditions; however, although the product obtained was given the formula $(C_5H_8)_2Fe(CO)_3$ on the basis of combustion analysis, no structure was assigned. No further work (apart from a US patent application[29]) was done in this area until 1958 when Hallam and Pauson[30] repeated Reihlen's work on butadiene, and soon after, Stone and coworkers[31] repeated the Reihlen isoprene experiment. Following Reihlen's procedure Stone and coworkers successfully prepared the complex $(C_5H_8)Fe(CO)_3$

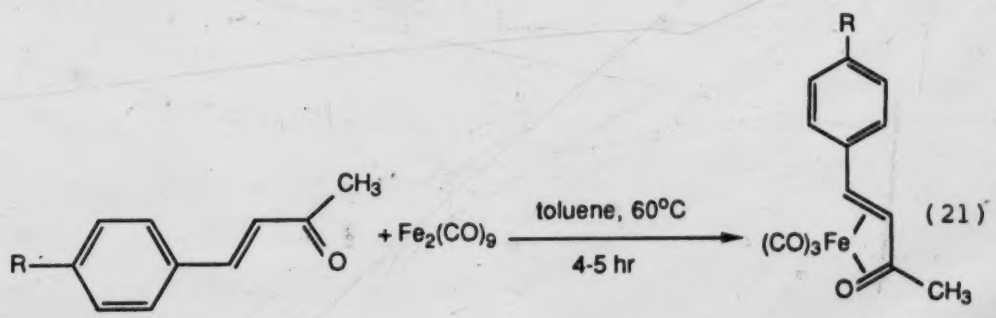
and speculated that this was indeed the same material Reihlen had prepared in 1930 but that it was contaminated by some side product produced by Diels-Alder dimerisation of isoprene 6 (eq. 20).

(20)

As well as repeating the thermal experiment of Reihlen, Stone and coworkers also prepared complex **30** via the photochemical reaction (sun lamp) of isoprene and $Fe(CO)_5$. Although the yield was low (1%), this technique has more recently become a rather general one since the yields have been much improved by use of more efficient ultraviolet light sources. For example, the photochemical preparation of the butadiene complex may now be accomplished in 65% yield.[32]

The high temperature (sealed tube) reaction of $Fe(CO)_5$ with dienes has also been improved by carrying out the reaction in an open system merely by refluxing the diene and $Fe(CO)_5$ in peroxide free di-n-butyl ether.[33] The open system has the advantage of allowing the carbon

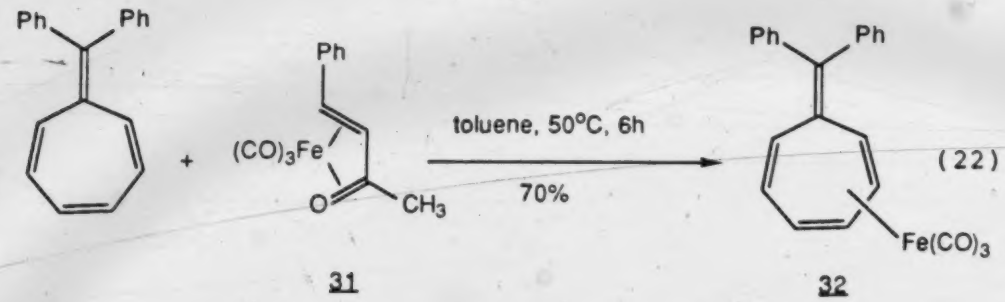
monoxide produced to escape irreversibly, thus shifting the reaction equilibrium to the product side. Obviously for this method to be successful the diene itself should be thermally stable at these high temperatures; if not, then either the aforementioned photochemical reaction may be employed, or a different iron carbonyl species can be used. For example, $Fe_3(CO)_{12}$ can be used to form diene complexes under milder conditions than $Fe(CO)_5$, usually by refluxing the diene and $Fe_3(CO)_{12}$ in benzene.[31,34] Milder conditions still are needed for reactions involving $Fe_2(CO)_9$, which will produce diene complexes at ca. 50-60°C, the conditions varying from complex to complex. The latter is also the species usually employed to prepare η^4-heterodiene complexes (eq. 21).[35]



31

Such complexes, particularly (benzylidene acetone)iron tricarbonyl **31** (R = H) have been used as $Fe(CO)_3$ transfer reagents to produce other diene iron carbonyl complexes which could not be produced via the thermal or

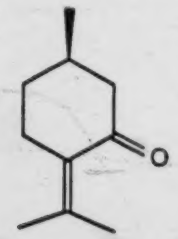
photochemical processes due to the sensitivity of the ligand to the reaction conditions, eg. the production of tricarbonyl(8,8-diphenylheptafulvene)iron **32** (eq. 22).[36]



(22)

31 **32**

Perhaps the most interesting application of heterodiene complexes lies in the preparation of optically active diene complexes, an area investigated by Birch and coworkers,[37] who prepared chiral heterodiene complexes using dienones such as (+)-pulegone, **33**, and (-)-3β-(acetyloxy)pregna-5,16-dien-20-one, **34**. These species were employed as transfer reagents to prepare chiral cyclohexadiene complexes, although only in moderate enantiomeric excess (the highest was 43% using **34**).



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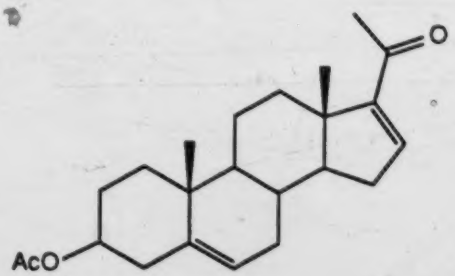
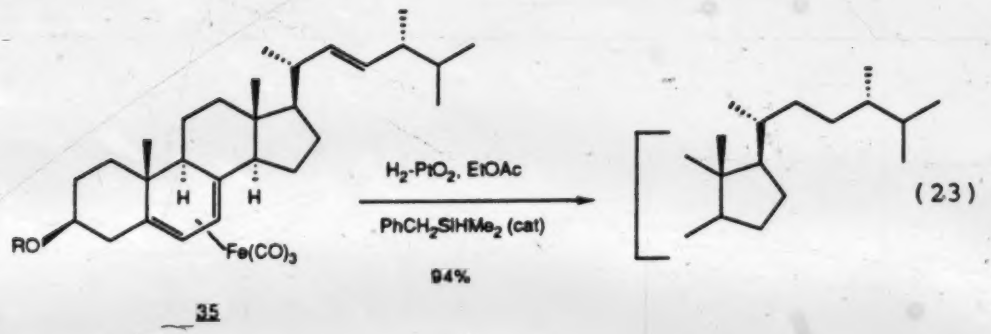


34

Another method for preparing diene iron carbonyl complexes was developed by Shvo and Hazum[38] and involves generation of the presumed $Fe(CO)_4$ intermediate by reaction of trimethylamine N-oxide (Me_3NO) with $Fe(CO)_5$ in the presence of the diene. The reaction is extremely rapid and is approximately 50% complete upon complete addition of the $Fe(CO)_5$, and is then completed by refluxing the reaction mixture for one hour.

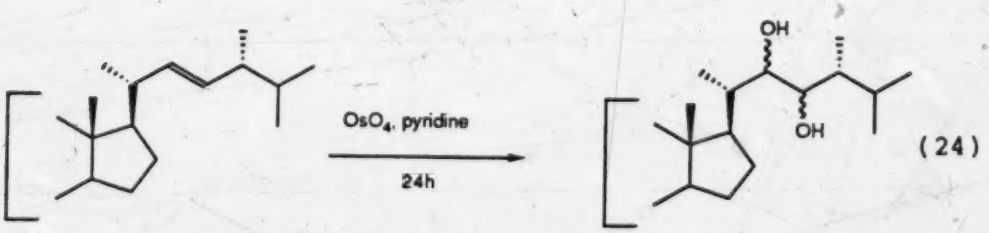
As mentioned previously, it is for their ability to modify the chemical behaviour of dienes that these complexes are of interest to organic chemists. These changes were first investigated by Hallam and Pauson[30] for the butadiene complex. They found that the complex was unaffected by hydrogen in the presence of Adam's catalyst (platinum oxide), conditions which would normally bring about the reduction of butadiene. Likewise the complex did not undergo a Diels-Alder reaction with maleic anhydride even after refluxing in benzene for 48 hours, and was only slightly affected by ozonolysis and lithium aluminum hydride reduction.

This inertness to hydrogenation was exploited by Barton and coworkers[39] as a means of protecting the diene functionality in ergosterylbenzoate **35** (R = PhCO) while the double bond in the side chain was hydrogenated (eq. 23).



35 (23)

Evans and coworkers[40] also demonstrated that in complex **35** (R = CH_3CO) the coordinated diene-$Fe(CO)_3$ unit was unaffected by treatment with osmium tetroxide, and oxidation occurred exclusively at the side chain double bond to produce diol **36** in 82% yield (eq. 24).

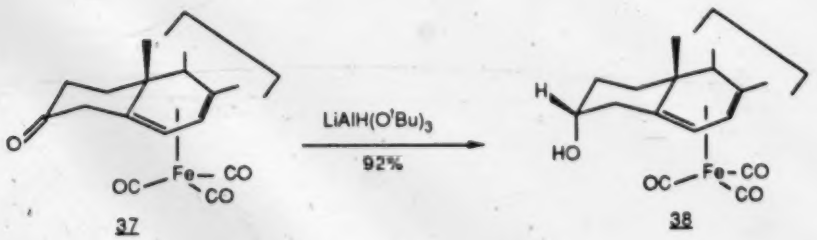


36 (24)

Similarly, reaction of **35** (R = $COCH_3$) with diborane, followed by workup with alkaline hydrogen peroxide left the diene $Fe(CO)_3$ unit intact, and produced a mixture of alcohols at the side chain double bond plus some reduction of the ester functionality.

Another interesting feature of diene-complex **35** is

that due to the crowded nature of the top (β) face of the steroid, the iron carbonyl moiety is located exclusively on the underside of the molecule and has an effect on the chemistry of the nearby 3 position. Barton and Patin[41] were thus able to bring about selective reduction of the ketone complex **37** (produced via N-chlorosuccinimide/dimethyl sulphide oxidation of **35** (R = H)), from the top face using the bulky reducing agent lithium hydridotri-t-butoxyaluminate ($LiAlH(OtBu)_3$), to give the previously unknown epimeric alcohol complex, tricarbonyl(epiergosterol)iron, **38**, in 92% yield (eq. 25).

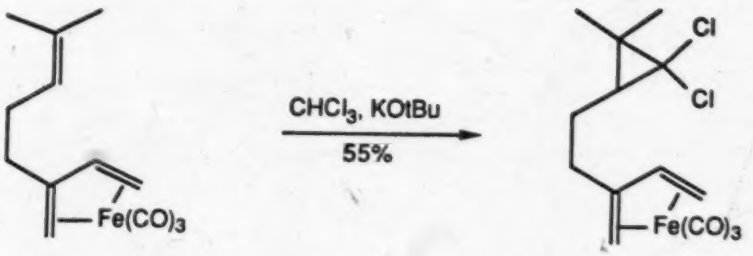


37 38 (25)

The steric bulk of the $Fe(CO)_3$ unit also has an effect on the rate of acetylation of **35** (R = H) and **38**, with the former being completely acetylated in one hour at room temperature, while the latter was unaffected.

The $Fe(CO)_3$ moiety is also unaffected by carbenes as evidenced by the formation of the cyclopropyl derivatives of myrceneirontricarbonyl **39** (eq. 26) and cyclohepta-

trieneirontricarbonyl **40** (eq. 27).[42]



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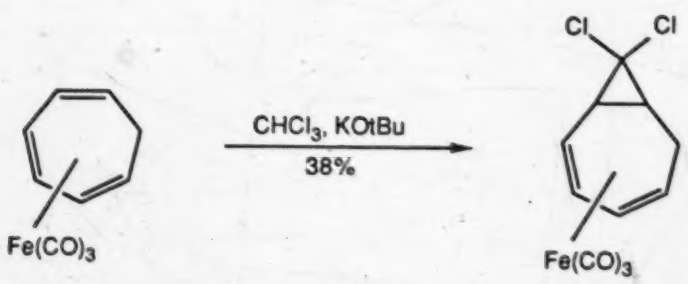
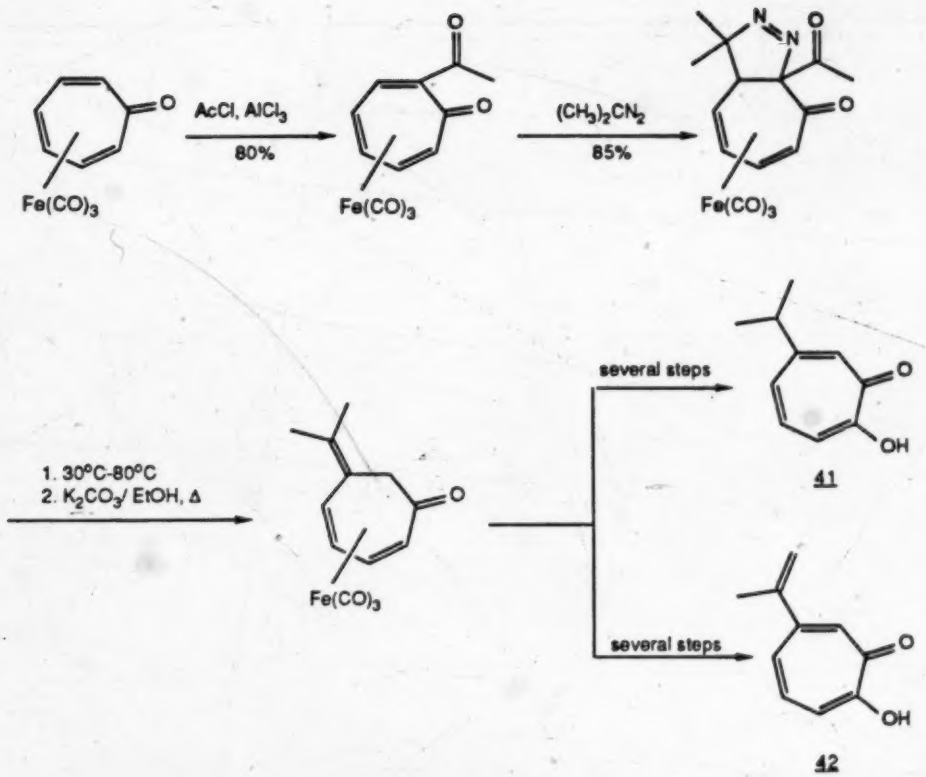


(27)

40

Complex **39** also undergoes selective acetylation at the side chain double bond under mild Friedel-Crafts conditions[43] even though acetylation of diene-$Fe(CO)_3$ complexes can be achieved fairly readily[44] (see Scheme III).

The ability to bring about acetylation of the uncomplexed double bond of a triene system has been used, in conjunction with the stability of the $Fe(CO)_3$ moiety to diazoalkanes, in the synthesis of the natural products β-Thujaplicin **41** and β-Dolabrin **42** (Scheme III).[45]

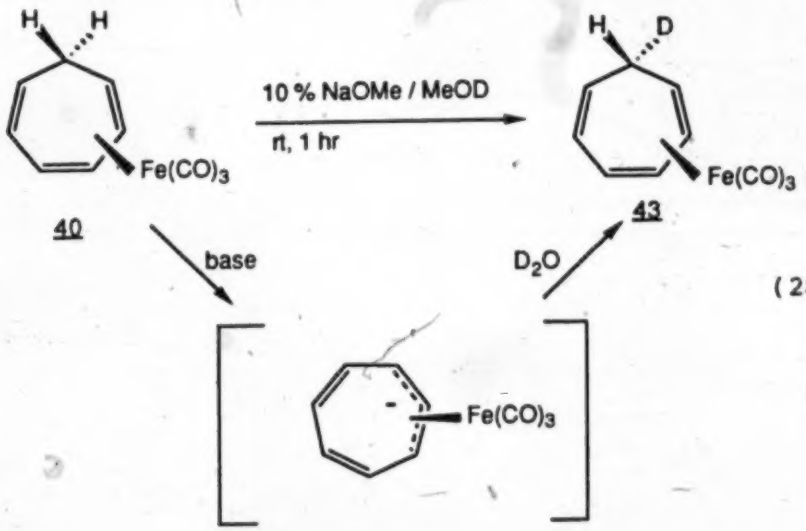


Scheme III

Complexation to a metal atom also has the ability to stabilise otherwise highly reactive or unstable species, thus allowing study and chemical modification of them (e.g. cycloheptatriene anion, cyclobutadiene and trimethylenemethane).

Although cycloheptatriene is very difficult to deprotonate (as evidenced by its high pK_a of 36[46]), the corresponding $Fe(CO)_3$ complex **40** readily undergoes deuterium exchange (10% NaOMe-MeOD, rt, 1 h) to produce

43,[47] and can be deprotonated by a variety of bases, eg. KOtBu,[42] KH[48] to produce the bright red anion 44 (eq. 28). The pK_a of complex 40 has been estimated to be 20;[42] thus, complexation brings about a 10^{16} fold increase in acidity.



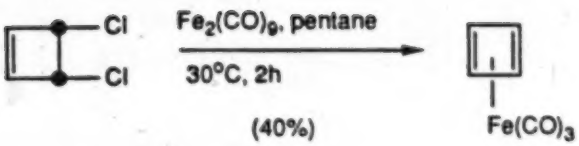
40 43 (28)

44

Similarly the highly reactive species cyclobutadiene, 45, has been stabilised as the iron carbonyl complex, 46

45

(eq. 29),[49] and numerous derivatives have been obtained



(29)

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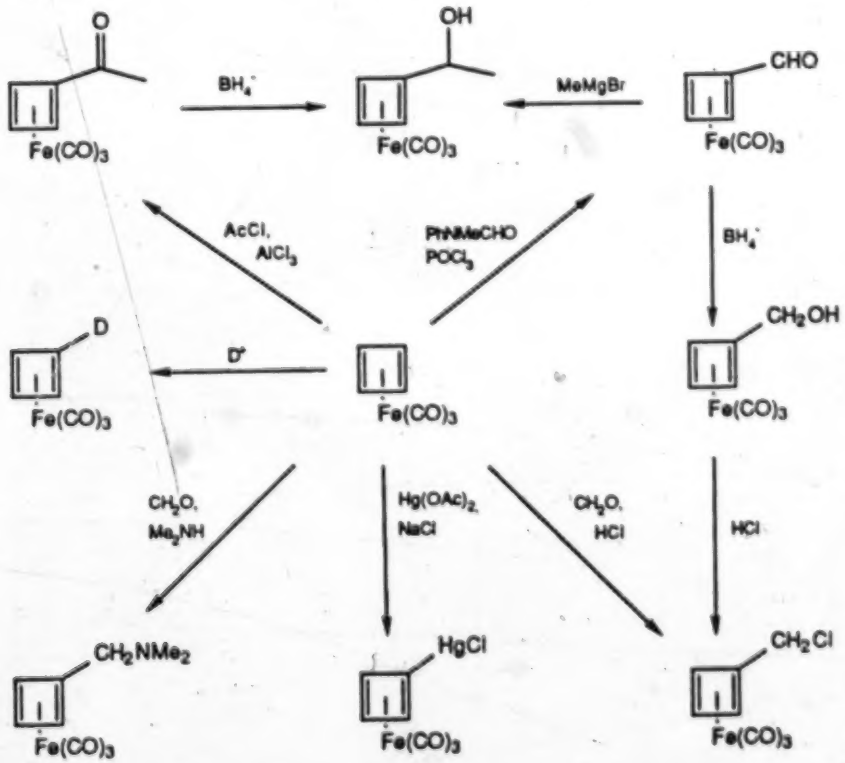
(Scheme IV),[50] again attesting to the stability of the $Fe(CO)_3$ moiety towards a large variety of chemical reagents and reaction conditions.

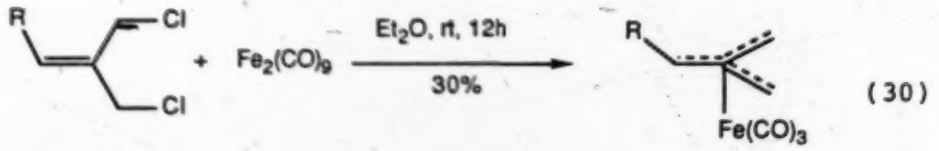


Scheme IV

Finally, the structurally interesting compound trimethylenemethane (TMM) **47** (R = H) and its derivatives

47

have also been stabilised using an iron tricarbonyl group. The parent complex **48** (R = H) was first reported in 1966[51] by the reaction of excess $Fe_2(CO)_9$ with 3-chloro-(2-chloromethyl)propene **49** (eq. 30).

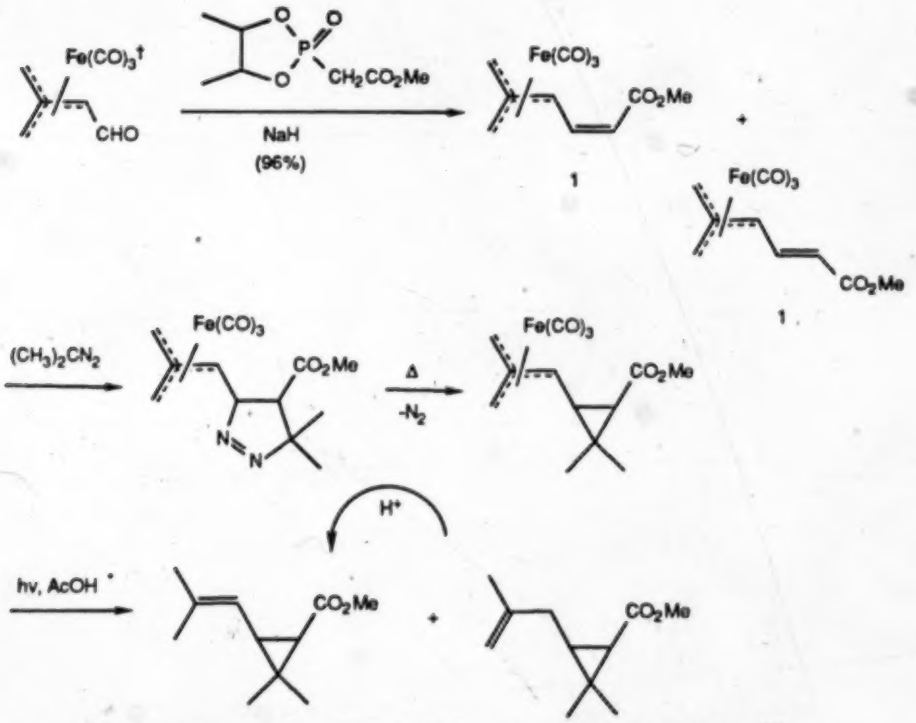


(30)

49 **48**

X-ray studies[52] of complex **48** (R = H) have shown that the organic ligand is not planar but slightly bent at the centre with the iron atom located nearest the central carbon atom and equidistant from the other three carbons. The equivalency of these three carbons, and the six protons attached to them, is demonstrated by the sharp singlet in the proton nmr spectrum. Numerous other

TMM-$Fe(CO)_3$ complexes have been reported subsequently (a review on the subject[53] lists at least 66 compounds of this type), and some have even found use as starting materials in organic syntheses, eg. preparation of chrysanthemates (Scheme V).[45]



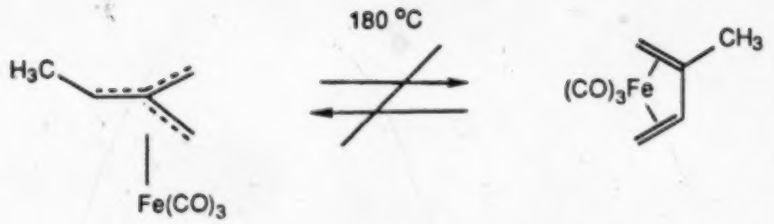
†. prepared from the corresponding alcohol complex by MnO_2 oxidation. (54)

•. reductive photodecomplextation (55)

Scheme V.

It should also be noted that methyltrimethylenemethane-$Fe(CO)_3$, **48** (R = CH_3), and isoprene-$Fe(CO)_3$, **30**, are structural isomers and have been shown to be non-

interconvertible on heating up to 180°C[56] (eq. 31).



(31)

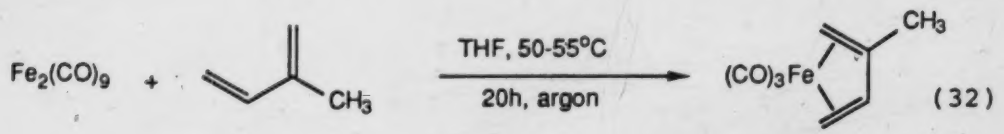
For these complexes to be of use to the organic chemist a means must be available for the removal of the iron tricarbonyl functionality without alteration of the organic ligand. Several such methods exist and these are now briefly described. Among the earliest oxidizing agents used were ferric(III) chloride and ceric ammonium nitrate (CAN),[57] and these are effective in most cases provided the free ligand is not particularly sensitive to the slightly acidic oxidation conditions. A milder technique using trimethylamine N-oxide was reported in 1974 by Shvo and Hazum,[58] and has found extensive use since then. Birch and Kelly recently reported[59] that ligand replacement (usually with phosphorous ligands) is possible using Me_3NO. Another ligand substitution/oxidation technique using alkaline hydrogen peroxide (H_2O_2/NaOH) was reported in 1979 by Davies[60] and again in 1983 by Franck-Neumann.[61] By controlling the amount of

reagent, stepwise replacement of carbon monoxide ligands by other ligands, eg. PPh_3, $P(OMe)_3$[60] can be accomplished. If a large excess of H_2O_2/NaOH is used, complete removal of the iron carbonyl moiety can be achieved and the results (75-95% yields)[61] are comparable to those using Me_3NO. A variety of other reagents have been used, eg. pyridinium chlorochromate,[62] copper(II) chloride[42], etc., although not as extensively as $FeCl_3$, CAN and Me_3NO. No particular reagent is universally applicable, and the "correct" one to use, plus the right oxidation conditions, is usually determined empirically.

During the course of this study the direct metallation of isoprene was recently reported[62a] using the specialised base combination lithium tetramethyl-piperidide-potassium tertiary butoxide. Nevertheless, this technique is intrinsically incapable of effecting chiral synthesis, which in principle is available by using transition metal complexes of (prochiral) unsymmetric dienes.

DISCUSSION

The starting complex, tricarbonyl(2-methyl-1,3-butadiene)iron, **30** (commonly called isoprene iron tricarbonyl), was prepared via the thermal reaction of nonacarbonyldiiron ($Fe_2(CO)_9$) with isoprene (eq. 32) using a modification[63] of the procedure of Dauben and Lorber.[64] Previous use of their procedure in our group



(32)

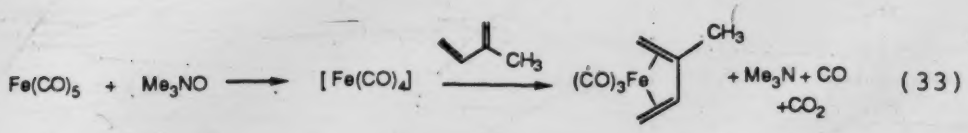
30

had produced the desired complex in only low yields (ca. 20-30%), and as a result, a number of changes were made.[63] Tetrahydrofuran (THF) was used in place of diethyl ether (in order to allow a higher reaction temperature), the reaction time was increased from five to ca. twenty hours, a large excess of isoprene was employed, and finally it was empirically determined that the yield was improved by increasing the volume of solvent used, good results being obtained with a concentration of

approximately 0.06N with respect to $Fe_2(CO)_9$. Even using this modified procedure, however, several of the early attempts resulted in only low yields (ca. 20%) and undesired side products. It was then found that the products were highly dependent upon the order in which the reagents were mixed. If $Fe_2(CO)_9$ was added to THF at room temperature, followed by isoprene, and the reaction continued in the normal manner, the desired complex **30** was produced in only low yield (ca. 20%), and the major product was an unidentified dark green oil. However, if isoprene was dissolved in THF, and the resulting solution warmed to the reaction temperature (50-55°C), followed by addition of the $Fe_2(CO)_9$, **30** was produced in good yield (59%). Cotton and Troup[65] have in fact shown that $Fe_2(CO)_9$ reacts with THF at 23°C under argon, but no products could be identified ("a...sample of diiron nonacarbonyl...stirred with 100 mL dry THF at 23°C under a flow of argon gas...acquired an orange-yellow colour immediately and then slowly (over a one hour period) changed to a deep red. IR spectra taken during this reaction sequence were very complex in the carbonyl stretching region (2100-1700 cm^{-1}) and have not been interpreted.")[65]

The procedure of Shvo and Hazum[38] was also briefly investigated, in which the reactive $Fe(CO)_4$ intermediate

is produced by reaction of trimethylamine N-oxide with $Fe(CO)_5$, and the intermediate is "internally" trapped by the double bond (eq. 33). This procedure did provide the



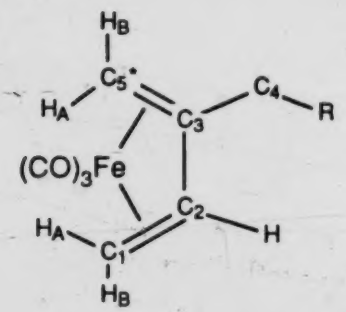
(33)

desired complex **30** in somewhat lower yield (41%) than the $Fe_2(CO)_9$ route, and also suffered from the same problems with by-products. It did, however, have the advantage of requiring a much shorter reaction time (ca. two hours) compared to the other procedure.

The base used for deprotonation of **30** was lithium 2,2,6,6-tetramethylpiperidide (LiTMP), generated by reaction of n-butyllithium with 2,2,6,6-tetramethylpiperidine (TMP) in the presence of hexamethylphosphoramide (HMPA) (10% v/v in THF).[63] The n-BuLi, TMP and HMPA were mixed in THF at -78°C for 30 minutes, after which time a solution of **30** in THF was added over a period of 30 minutes. The resulting solution was stirred for a further 30 minutes to ensure deprotonation of the complex before the electrophile was added, then the solution was allowed

to warm to room temperature overnight.

The products from these reactions were identified on the basis of their proton (^{1}H) nmr, infrared and mass spectra which, in the case of (η^4-diene)iron tricarbonyl complexes, are all particularly distinctive. The ^{1}H nmr of the complexes share the following features: (i) a broad one hydrogen triplet (J = 8 Hz) in the region δ5.1-5.4, corresponding to H2, **50**; (ii) a broad (sometimes



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*The numbering of this carbon atom varies depending on the nature of R

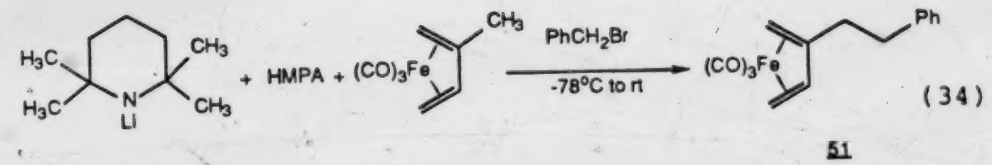
resolved) signal at ca. δ1.8 representing $H5_B$, in conjunction with a doublet of doublets (J = 7 and 2.3 Hz) at ca. δ1.7 for $H1_B$ (the "outer protons"); (iii) a similar set of signals further upfield at ca. δ0.3 and δ0.05 (J = 9 and 2.3 Hz) for $H5_A$ and $H1_A$ respectively (the "inner protons"). The dramatic upfield shift of the latter,

compared to their corresponding positions in the ^1H nmr spectra of the free dienes (*ca.* δ5.0) is believed to be caused by their proximity to the iron atom.[66]

The infrared spectra of the complexes are dominated by the signals for the carbonyl (C≡O) ligands. These appear as a sharp signal at *ca.* 2050 cm^{-1} and a broader signal (sometimes resolved) at *ca.* 1970 cm^{-1}; the former corresponds to the symmetrical stretching of the C≡O ligands and the latter to the unsymmetrical stretching. Other signals are usually much weaker but can occasionally be used for structure confirmation.

The mass spectra are also highly distinctive, with peaks resulting from the sequential loss of carbon monoxide from the molecular ion, usually ending up with a base peak corresponding to M^+-3CO. If the ionisation energy is sufficiently high the latter peak fragments further. In all the complexes the charge tends to reside on the fragment containing the iron atom due to its low ionisation potential (7.87 eV[67]), and an abundant fragment corresponding to m/e 56 (Fe) is often found in the high energy spectra.

Using the aforementioned technique the anion of 30 was generated and reacted with benzyl bromide to produce tricarbonyl(1,2,3,6-η-3-methylene-5-phenyl-1-pentene)iron 51, in 59% yield (eq. 34).



(34)

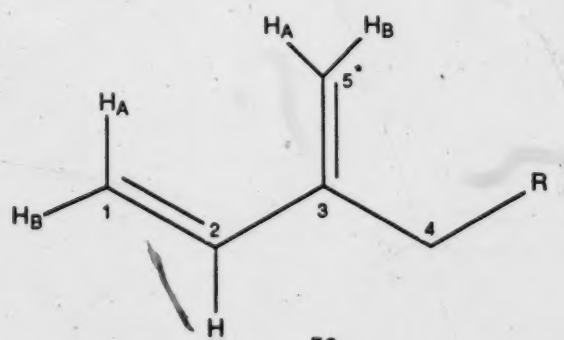
51

With this complex in hand its oxidation to the free 1,3-diene was investigated. The first oxidant studied was trimethylamine N-oxide (Me_3NO), the reagent developed by Shvo and Hazum.[58] This material is commercially available as its dihydrate (Aldrich) and although some groups have used it in this form,[68] it was felt that its activity would be increased by removing the water of crystallisation. This was achieved by refluxing the solid with dry toluene[69] in a Dean-Stark apparatus, then recrystallisation of the resulting solid from dry ethyl acetate. The oxidation technique involved heating (50-55°C) the complex in a dry aprotic solvent (both THF and toluene were used), with a large excess (14-15 equivalents of Me_3NO for several hours until TLC and/or infrared analysis (disappearance of C≡O signals) indicated that the reaction was complete. The onset of the reaction is accompanied by an evolution of gas (Me_3N and CO_2, eq. 35), and this phenomenon has been used by Birch[68]

$$(diene)Fe(CO)_3 + Me_3NO \xrightarrow{\Delta} diene + Me_3N + CO_2 + \text{"iron compounds"} \qquad (35)$$

to determine reaction temperatures for oxidations using this reagent. It should however be noted that the gas evolution is not quantitative.[58]

After workup and purification (see Experimental), the free 1,3-dienes were characterised by their ^1H nmr spectra, infrared spectra, elemental analyses and/or high resolution mass spectra. The ^1H nmr of the free dienes, like those of the complexes, have a number of characteristic signals including: (i) a one hydrogen doublet of doublets (J = 18 and 11 Hz) at ca. δ6.4 corresponding to H2, **52**; (ii) a one hydrogen doublet (J = 18 Hz) at ca. δ5.3 for $H1_A$; (iii) a one hydrogen doublet (J = 11 Hz) and two broad one hydrogen singlets at ca. δ5.0 for $H1_B$, $H5_A$ and $H5_B$ respectively.

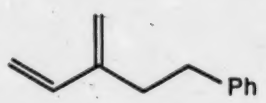


52

*Numbering varies depending on R.

The infrared spectra of the free dienes have two sets of signals in common: (i) absorptions at ca. 1650 and 1600 cm^{-1} resulting from C-C stretching, and (ii) absorptions at ca. 990 and 897 cm^{-1} for C-H out-of-plane deformations.[70]

Using the aforementioned technique complex **51** was oxidised to provide a pale yellow oil (55%) which was purified by flash chromatography (silica/toluene) to afford the known compound[6b,71] 3-methylene-5-phenyl-1-pentene **53** (45%).



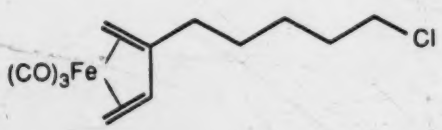
53

The oxidant ceric ammonium nitrate (CAN) was also investigated since this reagent had proven successful for several acyclic dienes in which Me_3NO had proven unsatisfactory.[72] The method employed was that of Greé and coworkers,[72] and involved reaction of the diene $Fe(CO)_3$ complex with CAN in methanol at -15°C. The addition of CAN in methanol solution (4-5 mole equivalents) to a solution of the diene-$Fe(CO)_3$ complex in methanol produces an immediate evolution of gas and the oxidations were monitored by measuring the volume of gas (in this case the reaction is quantitative producing 3 moles of carbon monoxide for each mole of diene $Fe(CO)_3$

complex[73]).

Using this procedure the oxidation of complex **51** resulted in a crude oil (87%) which was homogeneous by TLC analysis (silica/Skelly B), however purification resulted in the isolation of **53** (spectroscopically identical with that obtained previously) in only 40% yield. Washes of the chromatography column with more polar solvent systems (ether and ethyl acetate) did not result in isolation of any other identifiable products.

The anion of **30** was generated in the same manner and reacted with 1-bromo-4-chlorobutane in an attempt at differentiation between the two leaving groups. Examination of the product by mass spectroscopy indicated that the chloro complex **54** (M^+ = 298 for $C_{12}H_{15}{}^{35}ClFeO_3$ with a satellite at m/e 300 for $C_{12}H_{15}{}^{37}ClFeO_3$, ratio ca. 3:1), was the only product formed, although the yield was

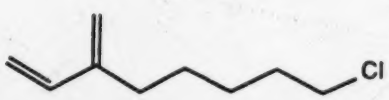


54

disappointingly low (38%). In an attempt to improve the yield, 1-bromo-4-chlorobutane was converted to 1-chloro-4-iodobutane in 82% yield via Finkelstein exchange with sodium iodide.[74] The reaction of this electrophile with

30 improved the yield of 54 to 51% along with the recovery of unreacted starting material (26%).

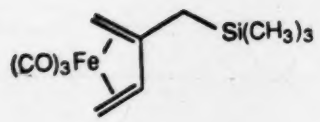
Oxidation of this complex with CAN in methanol resulted in a pale yellow oil (75%) whose infrared spectrum indicated a complete absence of carbonyl signals. The high resolution mass spectrum indicated a molecular weight of 158.0868 (calcd. for $C_9H_{15}{}^{35}Cl$: 158.0862). Purification by flash chromatography (silica/Skelly B) provided 8-chloro-3-methylene-1-octene 55 in 43% yield.



55

Reaction of the anion with chlorotrimethylsilane resulted in the isolation of an orange-brown oil (82%) but attempted purification by flash chromatography (silica/Skelly B) led to only 51% recovery of material. The main fraction was an (η^4-diene)iron tricarbonyl derivative (triplet at *ca.* δ5.2) and showed a strong signal at *ca.* δ0 for the trimethylsilyl functionality, but the expected trimethylsilyl derivative 56 could only be obtained in 2% yield.

This poor result, coupled with the low yield from the reaction with 1-bromo-4-chlorobutane, prompted a brief



56

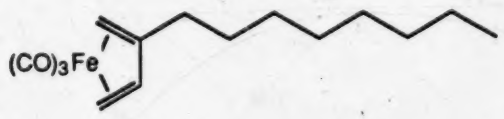
study of several reaction variables centering on the generation of LiTMP. An examination of the literature[75] indicated that the base could be prepared via reaction of TMP with either methyllithium or n-butyllithium but that the former, for some unexplained reason, gave better results. Methyllithium reacts with TMP relatively slowly at lower temperatures, and LiTMP is best prepared at room temperature.

Consequently we generated LiTMP at room temperature using methyllithium. A quantitative measure of base formation was also possible by collection of the methane evolved in a gas burette. The resulting LiTMP was then cooled to -78°C, followed by the addition of HMPA (10% v/v in ether). A solution of **30** in ether was added over a period of 30 minutes, stirred for a further 30 minutes, and then reacted with an electrophile. Using this procedure the yield of the benzylation product **51** improved to ca. 70%, the reaction with 1-bromo-4-chlorobutane produced complex **54** in an improved yield of 54% (along with recovery of starting material (21%)), and the reaction

of **30** with chlorotrimethylsilane produced complex **56** (55%) although technical difficulties were encountered in completely separating **56** from unreacted **30**.

In view of these results this method was adopted as a "standard" procedure for the generation of the anion of **30**, and the scope of the reaction was investigated using a variety of electrophiles.

The result of the reaction of **30** with 1-iodoheptane presented similar separation problems to those encountered in the chlorotrimethylsilane reaction. The crude mixture of unreacted **30**, 1-iodoheptane, and the desired product **57**, could only be partially separated by flash chromatography.



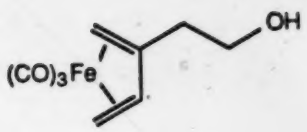
57

The yield of complex **57** was determined by nmr analysis to be 57%, along with 6% unreacted **30** and 7% 1-iodoheptane. Instead of further separation at this stage, the mixture was oxidised with CAN in methanol to give a crude mixture containing 1-iodoheptane and 3-methylene-1-undecene **58**. This could be separated by column chromatography (silica gel-silver nitrate, 2% ether:Skelly B), to provide **58** in 80% yield. The structure of **58** was confirmed by the following

58

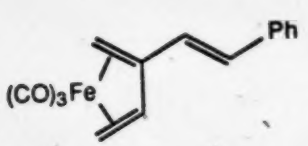
spectral data: molecular weight 166.1721 (calcd. for $C_{12}H_{22}$: 166.1722); ^1H nmr spectrum (400 MHz, $CDCl_3$) δ6.35 (d of d, J = 18 and 11 Hz, 1H, H2), 5.22 (doublet of triplets, J = 18 and 0.8 Hz, 1H, $H1_A$), 5.04 (d of d, J = 11 and 0.8 Hz,, 1H, $H1_B$), 4.99 (br s, 1H), 4.98 (br s, 1H, $H12_{AB}$), 2.20 (t, J = 8 Hz, 2H, H4), 1.48 (br m, 2H), 1.30 (br m, 10H, $(CH_2)_5$), 0.90 (m, 3H, CH_3).

In 1965 Schaap and coworkers[76] reported the use of paraformaldehyde as a substitute for the experimentally difficult to handle formaldehyde, in the conversion of organolithium compounds into the corresponding primary alcohols in good yields. Consequently the reaction of the anion of **30** with this electrophile was investigated. Solid paraformaldehyde was added to the solution of anion of **30** in ether/HMPA at -78°C and the mixture then warmed to room temperature. The crude product, a yellow-orange oil (99%) was purified by flash chromatography (silica/Skelly B, followed by SkellyB:ether (1:1)) to give the desired alcohol complex **59**, albeit only in low yield (32%), along with unreacted starting material (11%).

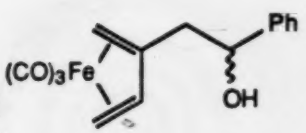


59

The reaction of the anion of **30** with benzaldehyde was also investigated. Flash chromatography (silica/toluene) of the crude product for this reaction resulted in four distinct fractions which were shown to contain, in order of elution, unreacted starting material (27%), a trace amount (4%) of a pale yellow solid identified by its ^1H nmr spectrum as **60** (^1H nmr spectrum (400 MHz, $CDCl_3$) δ8.07 (m, 2H, Ph), 7.59 (m, 1H, Ph), 7.49 (t, 2H, Ph), 5.37 (t, J = 8 Hz, 1H, H2), 4.10 (d, J = 16 Hz, 1H, H5), 3.88 (d, J = 16 Hz, 1H, H4), 1.84 (d of d, J = 2.5 and 1.5 Hz, 1H, $H6_B$), 1.78 (d of d, J = 7 and 2.5 Hz, 1H, $H1_B$), 0.48 (d of d, J = 3 and 1 Hz, 1H, $H6_A$), 0.26 (d of d, J = 9 and 2.5 Hz, 1H, $H1_A$), resulting from dehydration of **61**), recovered benzaldehyde (33%), and the desired product **61** (38%).



60

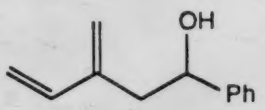


61

Although the latter appeared as a single spot in several TLC systems the ^1H nmr spectrum displayed two very similar sets of signals in a ratio of 3:2. The reaction was

repeated twice, and the yield of **61** could be increased to 85% using a longer reaction time (ca. 15 hours at -78°C). On each occasion however, the ratio of the aforementioned nmr signals was the same. It is believed that each set of signals belongs to one of the diastereomeric alcohols possible for **61**.

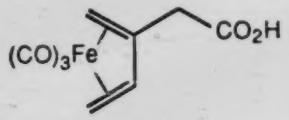
Oxidation of this complex with Me_3NO yielded an orange oil which was purified by flash chromatography to provide a 17% yield of 3-methylene-5-phenyl-penten-5-ol, **62**, with no other identifiable products. Oxidation with CAN in methanol yielded the crude alcohol **62** in 93% yield. Its identity was confirmed by high resolution mass spectroscopy 174.1043 (calcd. $C_{12}H_{14}O$: 174.1045) and by its ^1H nmr spectrum.



62

The reaction of organolithium compounds with carbon dioxide to produce carboxylic acids is often employed in synthesis. However, to obtain good yields it is important that the carbon dioxide is present in excess throughout the course of reaction (failure to do so can result in ketone and tertiary alcohol formation via further reaction of the organometallic).[77] This is normally achieved by

adding the organolithium to crushed dry ice or to a slurry of dry ice in a solvent. In this manner, addition of the anion of **30** to a slurry of dry ice in diethyl ether produced the carboxylic acid complex **63** in 89% yield after recrystallisation from ether/Skelly B (1:1).

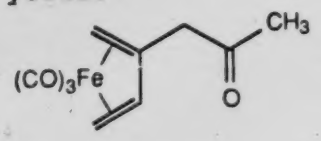


63

Oxidation of this complex with CAN resulted in a crude product which TLC analysis indicated was homogeneous. However attempted purification of this material resulted in a product which had an extremely complex ^1H nmr and mass spectra, and could not be identified. Oxidation of **63** with Me_3NO also proved unsuccessful, with the spectra (ir, nmr) of the crude reaction mixture being extremely complex.

The reaction of organolithium compounds with acid chlorides can in principle be used to produce ketones; in practise, however, the reaction must again be carefully controlled to prevent the product ketone from reacting with further organolithium to form the tertiary alcohol. The normal procedure was modified and the anion was gradually added via double ended needle, to an excess (3 mole equivalents) of acetyl chloride in ether at -78°C.

The resulting mixture was kept at -78°C and monitored by TLC, then quenched with water when all the starting material had been consumed (2 hours). This produced ketone **64** in 40% yield.

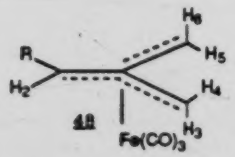


64

Attempts at oxidation of **64** with either Me_3NO or CAN were unsuccessful and produced products with complex, uninterpretable ^1H nmr and mass spectra.

Other less reactive electrophiles such as ethyl benzoate, benzonitrile and N,N-dimethylacetamide were also explored as substrates but in no case was there produced any identifiable ketone complexes (as evidenced by the lack of a signal at ca. 1720 cm^{-1} in the infrared spectra of the crude products). However, a new compound was isolated in moderate yield (53%) during the reaction of **30** with N,N-dimethylacetamide. The infrared spectrum, while showing no signal at ca. 1720 cm^{-1} did display signals at 2055 and 1980 cm^{-1} typical of an iron carbonyl complex. The ^1H nmr spectrum was unlike that of any of the isoprene complexes prepared previously, and showed the following signals: δ3.01 (doublet of quartets, J = 6.9 and 2.2 Hz, 1H), 2.48 (d, J = 4.4 Hz, 1H), 2.09 (d, J = 2.2 Hz, 1H), 1.69 (s, 1H), 1.55 (d, J = 4.4 Hz, 1H) and 1.28 (d, J =

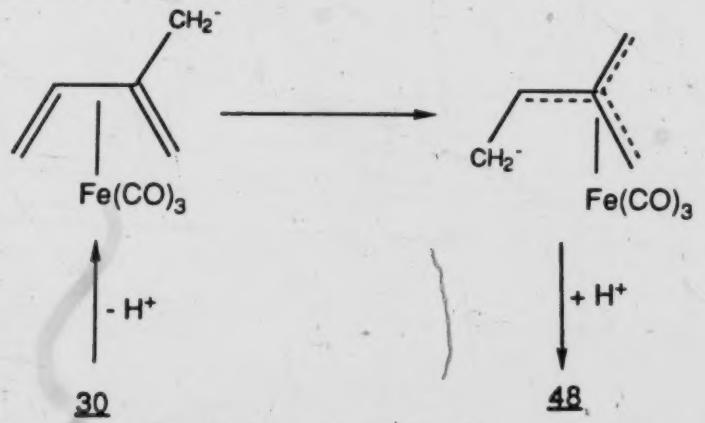
6.9 Hz, 3H). The ^{13}C nmr spectrum showed signals for five different carbon atoms at δ104, 73, 52, 50 and 15, suggesting that the compound was possibly a structural isomer of **30**. The spectrum also showed three distinct signals for the carbonyl ligands at δ212.0, 211.5 and 211.0, indicating a fairly high barrier to rotation of the carbonyl ligands. The latter is not the case for typical (η^4-diene)$Fe(CO)_3$ complexes where only one carbonyl is seen.[78] On this basis a trimethylenemethane structure **48** (R = CH_3) was assigned. Compounds of this type are known



to be sufficiently "rigid" to display three carbonyl signals in their ^{13}C spectra,[79] and to have distinctive, simple ^1H nmr spectra due to the limited amount of coupling between the protons, long range W coupling being the only type seen.[80] Confirmation of the structure was provided by a comparison with the reported ^1H nmr, and infrared spectra:[80] δ3.14 (H2), 2.51 (H6), 2.11 (H5), 1.77 (H4), 1.63 (H3), $J_{H_2H_5}$ = 2.5 Hz and $J_{H_3H_6}$ = 4.5 Hz; infrared 2058 and 1979 cm^{-1} (C≡O).

The possible thermal isomerisation of (isoprene)iron tricarbonyl to (methyltrimethylenemethane)iron tricarbonyl, and vice versa, was investigated by Aumann

and coworkers,[56] and was found not to occur even upon heating to 180°C (eq. 31). However, formation of the isoprene $Fe(CO)_3$ (or $MTMMFe(CO)_3$) anion (or cation) may in principle allow the "isomerisation" to occur via a formal redistribution of electrons, and a slight "migration" of the iron atom from a position under the central carbon atom in **48** to a position midway between carbon atoms 2 and 3 in compound **30** (eq. 38).



(38)

In order to investigate the relationship between the anion of complex **48** and that of complex **30**, the latter was generated in the usual manner, and the resulting solution divided into two aliquots. One portion was quenched with water at -78°C, whereas the other was warmed to room temperature prior to being quenched. During the warm-up period the latter underwent a series of colour changes from lemon-yellow (-78°C) through orange-yellow, finally attaining a deep orange-red colour at room temperature. The product from the "-78°C quench" was **30** (55%) and that

from the "room temperature quench" was **48** (32%), although nmr integration showed the latter contained ca. 8% of **30**.

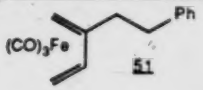
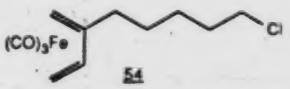
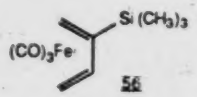
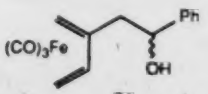
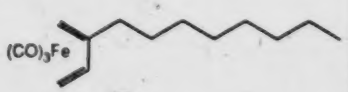
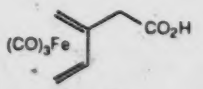
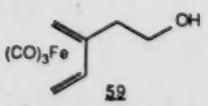
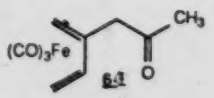
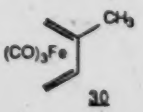
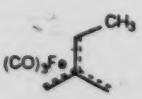
An attempt was made to determine if an alkylated derivative of **48** could be obtained by generating the anion of **30**, warming it to room temperature, then treating it with methyl iodide. However none of the desired (ethyltrimethylenemethane)iron tricarbonyl could be detected - the only identifiable product, after reduced pressure distillation of the crude mixture, was a small amount (<10%) of (methyltrimethylenemethane)iron tricarbonyl.

The results described above for the reaction of **30** with electrophiles are summarised in Table 1 and the results of the oxidation of the (η^4-diene)iron tricarbonyl complexes are summarised in Table 2.

In conclusion it has been shown that formation of the isoprene iron tricarbonyl complex allows deprotonation of the isoprene moiety to occur without polymerisation, and that the anion of the complex reacts with a variety of electrophiles to produce new iron tricarbonyl complexes in moderate to good yields. From these complexes the free dienes can be obtained via oxidative decomplexation using either ceric ammonium nitrate or trimethylamine N-oxide. Although the yields for the latter are low at present, it is hoped that future experimentation will provide these

TABLE 1.

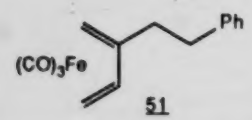
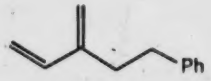
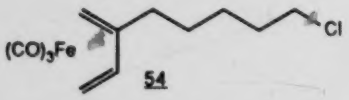
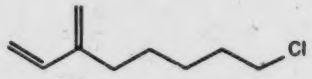
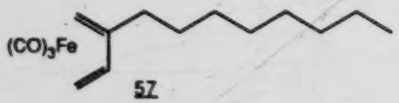
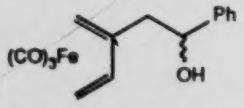
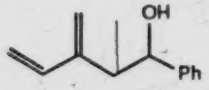
REACTION OF (ISOPRENE) IRON TRICARBONYL WITH ELECTROPHILES

ELECTROPHILE	PRODUCT	YIELD [a]
$PhCH_2Br$	 **51**	70% [b]
	 **54**	54%
$(CH_3)_3SiCl$	 **56**	55% [b]
PhCHO	 **61**	85% [c]
	 **57**	57% [b]
CO_2	 **63**	89%
$(CH_2O)_n$	 **59**	32%
CH_3COCl	 **64**	40%
H_2O -78 °C	 **30**	55%
H_2O room temp.	 **48**	29% [b]
$CH_3CON(CH_3)_2$	**49**	53%

a. Isolated yield.
b. Yield from NMR integration.
c. 3:2 mixture of isomers.

TABLE 2.

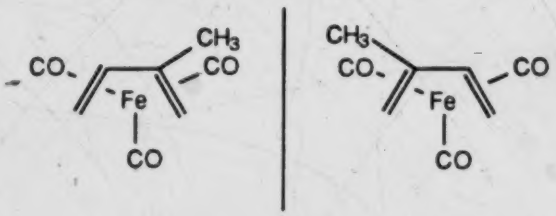
OXIDATION OF IRON TRICARBONYL COMPLEXES.

COMPLEX	OXIDANT	PRODUCT	YIELD (%)[a]
 51	Me_3NO	 53	45
	CAN		40
 54	CAN	 55	43
 57	CAN	58	80
 61	CAN	 62	93[b]
	Me_3NO		17

a. Isolated yield.
b. Crude yield.

dienes in better yields. If this can be achieved, this method, because of its brevity and easy availability of starting materials, offers a valuable alternative to current multistep procedures.

This method also has the advantage of providing the possibility of chiral synthesis. For example, complexation of an unsymmetrical (prochiral) diene to a transition metal produces a racemic mixture of two enantiomers. While no simple means exists for the resolution of such a racemic mixture, some prior work of Birch[37] has indicated that chiral **30** might be available



30

(via chirality transfer) using the reaction of suitable optically active heterodiene-$Fe(CO)_3$ complexes with isoprene, eg.

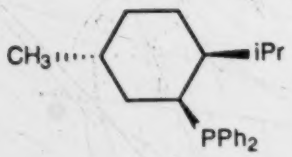
Prochiral Diene + (Chiral Auxiliary)$Fe(CO)_3$ →

(Chiral Diene)$Fe(CO)_3$ + Auxiliary

The interesting possibility exists, then, that

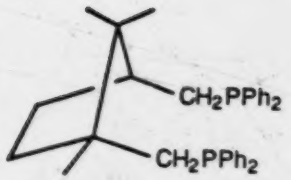
deprotonation of chiral **30** and subsequent alkylation could produce optically active isoprenoids by chiral induction.

The design of this method also offers other possibilities to be explored. For example, Howell and Thomas[81] have reported that substitution of one of the carbon monoxide ligands in a (1,3-cyclohexadiene)iron tricarbonyl complex with the chiral monodentate phosphorous ligand neomenthyldiphenyl phosphine **65**, led to modest chiral induction.

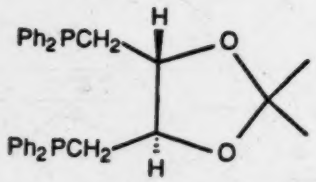


65

Substitution of carbonyl ligands with monodentate phosphorous ligands can be relatively easily achieved by treatment with Me_3NO, and Birch has reported[59] the replacement of a carbon monoxide ligand with **65** in 68% yield using this procedure. An alternative would be to use the technique of Davies[60] (H_2O_2/NaOH) to replace two of the carbonyl ligands with one of the many chiral bidentate phosphorous ligands developed in the field of chiral catalytic hydrogenation (eg. (+) CAMPHOS = (+) - (1R,3S) - 1,2,2-trimethyl-1,3-bis(diphenylphosphinomethyl)cyclopentane, **66** and (-)-DIOP = (-)-2,3-O-iso

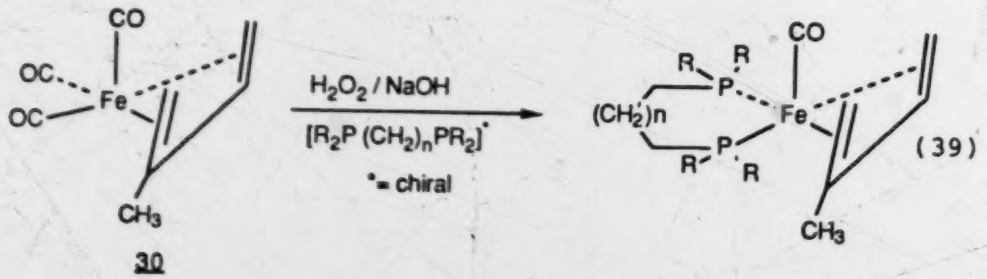


66



67

propylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane 67). By judicious choice of reagent, it may be possible to prepare suitable optically active derivatives for study (eq. 39) of chiral induction.



30 (39)

Finally, it has also been shown that the anion of the isoprene complex undergoes an interconversion on warming from -78°C to room temperature to produce, after hydrolysis, the isomeric complex (methyltrimethylene-methane)iron tricarbonyl. It remains for future work to investigate this phenomenon in greater detail in achiral, and possibly chiral form. The consequences of such a study would be of interest, both from the standpoint of structure and synthesis.

EXPERIMENTAL

General Procedures

Nuclear magnetic resonance (nmr) spectra were run on a Bruker WP-80, Bruker WH-200, Bruker AM-300 or Bruker WH-400 spectrometers (as indicated), using deuterated chloroform ($CDCl_3$), and tetramethylsilane (TMS) as an internal standard. Chemical shifts are reported as δ values in parts per million downfield from TMS, followed by the multiplicity, coupling constant(s) in Hertz, number of hydrogens and signal assignment. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, d of d = doublet of doublets, m = multiplet, br = broad. H_A and H_B refer, respectively, to the inner and outer protons of the diene unit as outlined in the Discussion (see page 35), and typified by structure 50.

Infrared spectra (ir) were recorded on a Nicolet 7199 FTIR in the manner indicated. The following abbreviations are used: s = strong, m = medium, w = weak, sh = shoulder.

Low resolution mass spectra of the iron complexes were recorded on an AEI MS12, and exact mass measurements on a Kratos MS50 spectrometer. Both are reported as m/e (relative intensity).

Analyses were performed by the Microanalytical Laboratory of this department.

Melting points were measured on a Reichert hot stage apparatus and are uncorrected.

Commercial methyllithium in diethyl ether (Aldrich), was standardised by titration using diphenylacetic acid as an indicator.[82]

All reactions involving the tricarbonyl(diene)iron complexes were performed under argon, using standard techniques.[83] Glassware was oven-dried at 140°C for several hours. All solvents were distilled under argon (purified further by passage through a tower of reduced BASF catalyst R3-11 and a drying tower filled with Drierite and sodium hydroxide pellets); diethyl ether and tetrahydrofuran were refluxed over potassium, benzophenone added and distilled; toluene was refluxed over sodium, benzophenone added, and distilled; ethyl acetate and Skellysolve B were distilled from calcium hydride, 2,2,6,6-tetramethylpiperidine (TMP) was dried over sodium hydroxide pellets, filtered, and distilled at atmospheric pressure,[75] then stored in the dark under argon. Trimethylamine oxide dihydrate (Aldrich) was dehydrated by the azeotropic removal of water with toluene,[69] followed by recrystallisation, under argon, from ethyl acetate. All electrophiles were purified by standard procedures.[84]

Flash chromatography was performed using MN Silica Gel 60 minus 200 mesh ASTM (Macherey Nagel and Co.), according to the technique of Still.[85] Thin layer chromatography (TLC) was carried out using precoated Merck Silica Gel 60 F254 plates. Compounds were visualised by ultraviolet light and/or iodine vapour. Alumina (II) refers to aluminum oxide Brockmann activity (II) manufactured by British Drug House (BDH).

Preparation of Tricarbonyl(2-methyl-1,3-butadiene)iron

Method A:[63] A 2 litre 3-neck round bottom flask was oven-dried, capped with rubber septa and cooled under a stream of argon. One litre of freshly distilled tetrahydrofuran (THF) was transferred to the flask via double ended needle from a solvent still, followed by 70 mL (700 mmol) of freshly distilled isoprene. The flask was then fitted with a water condenser topped by a dry-ice condenser, a magnetic stirring bar and a thermometer. The solution was slowly warmed, with stirring, to 50-55° (internal temperature), the remaining rubber septum was replaced with a Schlenk tube containing 23.79 g (65.3 mmol) diiron nonocarbonyl which was added to the solution. The mixture was kept at this temperature for 20 hours, then cooled to room temperature, filtered, and evaporated in vacuo using a rotary evaporator (water

aspirator). The resulting dark orange-brown oil was chromatographed over alumina (II), eluting with Skellysolve B, then distilled to yield tricarbonyl(2-methyl-1,3-butadiene)iron **30** (8.01 g, 59%), as an orange oil bp 63-65°C (6.5 torr);[86] ^{1}H nmr (400 MHz, $CDCl_3$) δ5.28 (t, J = 8 Hz, 1H, H3), 2.18 (s, 3H, CH_3), 1.84 (t, J = 1.5 Hz, 1H, $H1_B$), 1.65 (d of d, J = 7 and 2.4 Hz, 1H, $H4_B$), 0.32 (d of d, J = 1.5 and 0.8 Hz, 1H, $H1_A$), 0.05 (d of d, J = 9 and 2.4 Hz, 1H, $H4_A$); ^{13}C nmr (75.5 MHz, $CDCl_3$) δ211.59, 103.11, 84.77, 43.90, 38.05, 22.90; IR (liquid film) 2058 (s), 1990 (s), 1966 (s) cm^{-1}; MS, m/e (relative intensity) 208(43) M^+ (for $C_8H_8FeO_3^+$), 180(36), 152(24), 124(100), 108(5), 96(14), 84(21), 82(20), 56(65).

Method B: A slurry of 6.22 g (82.8 mmol) anhydrous trimethylamine oxide in 60 mL dry THF was placed in a 100 mL 3-neck R.B. flask equipped with an addition funnel, magnetic stirring bar, septum inlet, and a dry-ice condenser with an outlet to a mineral oil bubbler. The mixture was cooled to -78°C and 2.1 mL (21 mmol) freshly distilled isoprene were added via syringe, followed by the dropwise addition, with stirring, of 5.4 mL (41 mmol) iron pentacarbonyl. When the addition was complete the cooling bath was removed and the solution was warmed to room temperature over a period of 1 h, followed by one hour of reflux. The solution was cooled to room temperature,

filtered, and concentrated on a rotary evaporator. The resulting oil was purified by flash chromatography (silica/Skelly B), to yield tricarbonyl(2-methyl-1,3-butadiene)iron **30** (1.75 g, 41%) with spectral properties identical to those of the material obtained via method A.

General Procedure for the Generation of the Anion of Tricarbonyl(2-methyl-1,3-butadiene)iron, and its Reaction with Benzyl Bromide:

Into an oven-dried 100 mL 3-neck R.B. flask, equipped with an addition funnel, septum inlet, low temperature thermometer, and magnetic stirring bar, was placed dry diethyl ether (36 mL). To this was added 2,2,6,6-tetramethylpiperidine (0.58 mL, 3.4 mmol), followed by a solution of methyllithium in diethyl ether (2.4 mL, 3.6 mmol). The solution was stirred at room temperature until methane evolution ceased (approximately 10 min), and then cooled to -60°C (internal temperature), at which point hexamethylphosphoramide (HMPA) (4 mL, 10% v/v with respect to ether), was added. To this solution of lithium 2,2,6,6-tetramethylpiperidide/HMPA was introduced tricarbonyl(2-methyl-1,3-butadiene)iron (628 mg, 3.02 mmol) in ether (5 mL) over a period of 30 min, and the funnel rinsed with ether (5 mL). This solution was stirred for a further 30 min after which time benzyl

bromide (0.57 mL, 4.8 mmol) was added. The reaction mixture was stirred for one hour at -78°C, then allowed to warm to room temperature overnight. This solution was poured into brine, the ether layer was separated, and the aqueous layer extracted with Skelly B (4×50 mL). The combined ether-Skelly B extract was successively washed with water (25 mL), then brine (25 mL), dried over anhydrous magnesium sulphate, and concentrated on a rotary evaporator (water aspirator; bath temperature approximately 30°C). The resulting oil was purified by flash chromatography (silica/Skelly B) to give, in order of elution, recovered starting material (62 mg, 10%), and product (707 mg, 79%). The nmr spectrum of the latter showed it to be 11% benzyl bromide and 89% desired product. The overall yield of tricarbonyl(1,2,3,6-η-3-methylene-5-phenyl-1-pentene)iron 51 was 70%. ^{1}H nmr (200 MHz, $CDCl_3$) δ7.28 (m, 5H, Ph-), 5.20 (t, J = 8 Hz, 1H, H2), 3.00 (m, 2H, $-CH_2-$), 2.65 (m, 2H, $-CH_2-$), 1.80 (brs, 1H, $H6_B$), 1.68 (d of d, J = 7 and 2.5 Hz, 1H, $H1_B$), 0.29 (d, J = 1.5 Hz, 1H, $H6_A$), 0.10 (d of d, J = 9 and 2.5 Hz, 1H, $H1_A$); IR (liquid film) 2046 (s), 1963 (s) cm^{-1}; MS m/e (relative intensity) 298(3), M^+ (for $C_{15}H_{14}FeO_3^+$), 270(3), 242(4), 214(100), 158(2), 91(18), 65(3), 56(14), 39(2).

Reaction of Complex 30 with 1-Bromo-4-chlorobutane:

The anion of the starting complex was generated as described above from 2,2,6,6-TMP (0.81 mL, 4.8 mmol), methyllithium (3.2 mL, 4.8 mmol), and 30 (652 mg, 3.1 mmol). 1-Bromo-4-chlorobutane (0.64 mL, 5.6 mmol) was introduced via syringe, and the solution stirred for 35 min at -60°C (internal temperature), then warmed to room temperature and stirred for a further 45 min. The reaction was quenched with brine, the layers separated, and the aqueous layer extracted with Skelly B. The combined ether-Skelly B extract was successively washed with water, then brine, dried over magnesium sulphate and concentrated on a rotary evaporator. The resulting crude oil was purified by flash chromatography (silica/Skelly B), to yield starting material (136 mg, 21%), and tricarbonyl(1,2,3,9-η-8-chloro-3-methylene-1-octene)iron 54 (497 mg, 54%). ^{1}H nmr (400 MHz, $CDCl_3$) δ5.24 (t, J = 8 Hz, 1H, H2), 3.54 (t, J = 6.5 Hz, 2H, $-CH_2-$), 2.38 (m, 1H, H4), 2.25 (m, 1H, H4), 1.68 (m, 8H, H5,6,7,1_B, 9_B), [expansion: 1.78 (t, J = 2 Hz, $H9_B$), 1.65 (d of d, J = 7 and 2 Hz, 1H, $H1_B$)], 0.26 (d, J = 2 Hz, 1H, $H9_A$), 0.05 (d of d, J = 9 and 2 Hz, 1H, $H1_A$); IR ($CDCl_3$ cast) 2047 (s), 1985 (s) cm^{-1}; MS m/e (relative intensity) 300(7) M^+ (for $C_{12}H_{15}{}^{37}ClFeO_3{}^+$), 298(20) M^+ (for $C_{12}H_{15}{}^{35}ClFeO_3{}^+$), 270(12), 242(43), 214(100), 178(100), 158(27), 124(81), 91(51), 56(95).

Reaction of Complex 30 with Chlorotrimethylsilane:

Metallation of the parent complex was accomplished in the manner previously described using 2,2,6,6-TMP (0.64 mL, 3.8 mmol), methyllithium (2.5 mL, 3.8 mmol), and complex **30** (658 mg, 3.2 mmol). A solution of chlorotrimethylsilane (0.60 mL, 4.8 mmol) in ether (5 mL) was added and the resulting solution stirred for 45 min at -78°C and then allowed to warm to room temperature overnight. Workup of the reaction was as described in the general procedure. The yellow oil obtained was partially purified by fractional bulb-to-bulb distillation (using two receiver bulbs). This technique yielded two fractions; A, 178 mg bp 58-62°C (11 torr) and B, 337 mg bp 68-75°C (11 torr). Fraction A (by nmr) was 10% starting material, 90% tricarbonyl(1,2,3,5-η-3-methylene-4-trimethylsilylbutene)-iron **56**; fraction B was pure **56**. The overall yield of **56** was 55%. ^{1}H nmr (200 MHz, $CDCl_3$) δ5.14 (t, J = 8 Hz, 1H, H2), 2.02 (d, J = 13 Hz, 1H, H4), 1.75 (t, J = 2 Hz, 1H, $H5_B$), 1.65 (d of d, J = 7 and 2 Hz, 1H, $H1_B$), 1.63 (d, J = 13 Hz, 1H, H4), 0.29 (d of d, J = 2 and 1 Hz, 1H, $H5_A$), 0.13 (s, 9H, $(CH_3)_3Si$), 0.06 (d of d, J = 9 and 2 Hz, 1H, $H1_A$); IR ($CDCl_3$ cast) 2017 (s), 1965 (s) cm^{-1}; MS m/e (relative intensity) 280(14) M^+ (for $C_{11}H_{16}FeSiO_3^+$), 252(13), 224(35), 196(100), 73(16), 56(12).

Reaction of Complex 30 with Benzaldehyde:

The anion was generated from complex **30** (549 mg, 2.64 mmol), 2,2,6,6-TMP (0.55 mL, 3.3 mmol), and methyllithium (2.1 mL, 3.3 mmol) in the manner previously described. Benzaldehyde (0.40 mL, 4.0 mmol) was added via syringe at -78°C. The solution was stirred at this temperature for one hour and then warmed to room temperature and quenched with brine. The reaction mixture was then worked up in the usual manner using ether for the extraction of the aqueous phase in place of Skelly B. The residue remaining, after concentration (rotary evaporator) was purified by flash chromatography (silica/toluene) to yield, in order of elution, unreacted starting material (150 mg, 27%), tricarbonyl(1,2,3,6-η-3-methylene-5-phenyl-1,4-pentadiene)iron, **60** (29 mg, 4%), a pale yellow solid (mp 98-100°C). ^{1}H nmr (400 MHz, $CDCl_3$) δ8.01 (m, 2H), 7.59 (m, 1H) and 7.49 (t, 2H, Ph), 5.37 (t, J = 8 Hz, 1H, H2), 4.10 (d, J = 16 Hz, 1H, H5), 3.88 (d, J = 16 Hz, 1H, H4), 1.84 (d of d, J = 2.5 and 1.5 Hz, 1H, $H6_B$), 1.78 (d of d, J = 7 and 2.5 Hz, 1H, $H1_B$), 0.48 (d of d, J = 3 and 1 Hz, 1H, $H6_A$), 0.26 (d of d, J = 9 and 2.5 Hz, 1H, $H1_A$); benzaldehyde (140 mg, 33%), and impure alcohol. The latter was purified by flash chromatography (silica/40% ether:Skelly B), to give tricarbonyl(1,2,3,6-η-methylene-

5-phenyl-1-penten-5-ol)iron, **61** (318 mg, 38%) as a mixture of isomers (approximately 3:2). ^{1}H nmr (400 MHz, $CDCl_3$) δ7.31 (m, 5H, Ph), 5.31 (t, J = 8 Hz, 0.3H, H2), 5.14 (t, J = 8 Hz, 0.7H, H2), 4.97 and 4.92 (doublet of multiplets, 1H, H5), 2.84 (m, 1H, H4), 2.67 (m, 0.6H, H4) and 2.46 (m, 0.4H, H4), 2.21 (d, J = 3 Hz, 1H, OH), 1.78 (t, J = 2 Hz, 0.6H, $H6_B$), 1.74 and 1.71 (t + d of d, J = 2 Hz and J = 7 and 2.5 Hz, 0.8H, $H6_B$ + $H1_B$), 1.61 (d of d, J = 7 and 2.5 Hz, 0.6H, $H1_B$), 0.28 (d, J = 2 Hz, 0.6H, $H6_A$), 0.24 (d, J = 2 Hz, 0.4H, $H6_A$), 0.12 (d of d, J = 9 and 2.5 Hz, 0.4H, $H1_A$), 0.05 (d of d, J = 9 and 2.5 Hz, 0.6H, $H1_A$); ^{1}H nmr (D_2O exchange) δ4.97 (d of d, J = 14 and 11 Hz), 4.92 (d of d, J = 17.5 and 8.5 Hz); ^{13}C nmr (100 MHz, acetone-d_6) δ212.82 (C≡O), 145.73 (C_1', Ph), 128.94, 128.90, 127.96, 127.02, 126.86 ($C_{2'-6'}$, Ph), 104.79 (C^3), 87.82, 87.00 (C^2), 75.76, 75.54 (C^5), 49.27, 48.78, 45.50, 39.28 (C' and C^6), 30.37, 30.19 (C^4); IR (film) 334 (broad, w), 2049 (s), 1963 (s), 1040 (w), 755 (w), 701 (w) cm^{-1}; MS m/e (relative intensity) 314(0.2) M^+ (for $C_{15}H_{14}FeO_4$), 286(9), 258(4), 230(100), 212(34), 56(23).

The reaction was repeated with the solution of the anion and benzaldehyde being kept at -78°C overnight, and then warmed to room temperature and worked up in the previous manner. This yielded, after chromatography, unreacted starting material (72 mg, 8%) and **61** (1.10 g,

85%) in the same ratio of isomers (by nmr) as previously observed.

Reaction of Complex 30 with 1-Iodoheptane:

1-Iodoheptane (0.45 mL, 2.8 mmol) was added via syringe to a solution of the anion of **30** (573 mg, 2.75 mmol) in ether/HMPA (40 mL). The resulting solution was stirred for one hour at -78°C, then warmed to room temperature and left overnight. The reaction mixture was poured into ice-cold water (150 mL), followed by workup in the usual manner (extraction with Skelly B). The resulting crude oil was purified by flash chromatography (silica/Skelly B) into two fractions. The first (386 mg), was shown by nmr to be a mixture of 1-iodoheptane (7%) and product (93%), and the second (177 mg) was 71% product, 21% starting complex and 8% 1-iodoheptane. The overall yield (by nmr integration) of tricarbonyl(1,2,3,12-η-3-methylene-1-undecene)iron, **57**, was (483 mg, 57%). ^{1}H nmr (400 MHz, $CDCl_3$) δ5.22 (t, J = 8 Hz, 1H, H2), 2.30 (m, 2H, H4), 1.80 (t, J = 2.5 Hz, 1H, $H12_B$), 1.66 (d of d, J = 7 and 2.5 Hz, 1H, $H1_B$), 1.42 and 1.32 (m, 12H, H5→10), 0.90 (t, J = 7.5 Hz, 1H, H11), 0.28 (d, J = 1.5 Hz, 1H, $H12_A$), 0.06 (d of d, J = 9 and 2.5 Hz, 1H, $H1_A$); IR (neat film) 2949 (sh), 2928 (m), 2847 (m), 2049 (s), 1970 (s) cm^{-1}; MS m/e (relative intensity) 306(15) M^+ (for $C_{15}H_{22}FeO_3$),

278(8), 250(7), 222(96), 166(10), 152(49), 138(21), 124(75), 56(100).

Reaction of Complex 30 with Carbon Dioxide:

The anion of complex **30** (866 mg, 4.16 mmol) was generated as before using 54 mL of ether and 6 mL of HMPA as the solvent system. After stirring for 30 min at -78°C the solution was added via double ended needle to a slurry of dry ice/ether in a 1 L R.B. flask, fitted with a rubber septum and a large gauge needle outlet to a mineral oil bubbler. The mixture was allowed to warm to room temperature overnight with the carbon dioxide escaping through the bubbler. Ice cold water (100 mL) was added, followed by the addition of concentrated hydrochloric acid (0.34 mL, 4.2 mmol) in water (1 mL). The mixture was then acidified with 1N HCl until the aqueous layer had a pH of 2 (this is best performed with the mixture in a separatory funnel). The ether layer was separated, and the aqueous fraction extracted further with ether (3×75 mL). The combined ether extract was successively washed with water (50 mL), brine (50 mL), and dried over $MgSO_4$. The ether was removed on a rotary evaporator to give a crude pale yellow solid. This was recrystallised from ether-Skelly B (1:1) to yield tricarbonyl(3,6,4,5-η-3-methylene-4-pentenoic acid)iron **63** (929 mg, 89%) as a pale yellow

solid, mp 75-77°C. ^{1}H nmr (400 MHz, $CDCl_3$) δ9.47 (very broad s, 1H, $CO_2\underline{H}$), 5.42 (t, J = 8 Hz, 1H, H4), 3.48 (d, J = 16 Hz, 1H, H2), 3.27 (d, J = 16 Hz, 1H, H2), 1.85 (brs, 1H, $H6_B$), 1.77 (d of d, J = 7 and 2.5 Hz, 1H, $H5_B$), 0.39 (brd, J = 2.3 Hz, 1H, $H6_A$), 0.19 (d of d, J = 9 and 2.5 Hz, 1H, $H5_A$); IR ($CHCl_3$ cast) 3239-2525 (s), 2062 (s), 1989-1953 (s), 1710 (s), 1412 (m) cm^{-1}; MS m/e (relative intensity) 244(14) M^+-CO (M^+ for $C_9H_8FeO_5$ absent), 196(54), 168(84), 140(100), 122(37), 84(32), 56(98), 28(98).

Reaction of Complex 30 with Paraformaldehyde:

A solution of the anion of **30** (603 mg, 2.90 mmol) was formed as before. Solid paraformaldehyde (0.44 g, 14.7 mmol) was added and the mixture stirred for 2 hours at -78°C, then warmed to room temperature and left stirring overnight. The reaction mixture was poured into saturated ammonium chloride (200 mL) then worked up in the usual manner (extraction with ether). The crude orange-yellow oil was purified by flash chromatography, eluting with Skelly B followed by ether-Skelly B (1:1). This resulted in recovered starting material (65 mg, 11%), and tricarbonyl(1,2,3,6-η-3-methylene-1-penten-5-ol)iron **59** (220 mg, 32%). ^{1}H nmr (400 MHz, $CDCl_3$) δ5.38 (t, J = 8 Hz, 1H, H2), 3.96 (m, 2H, CH_2), 2.68 (m, 1H, H4), 2.48 (m, 1H,

H4), 1.83 (t, J = 2 Hz, 1H, $H6_B$), 1.72 (d of d, J = 7 and 2.5 Hz, 1H, $H1_B$), 1.65 (brs, 1H, OH), 0.31 (d, J = 2 Hz, 1H, $H6_A$), 0.11 (d of d, J = 9 and 2.5 Hz, 1H, $H1_A$); IR (neat film) 3340 (m, broad), 2055 (s), 1971 (s), 1050 (m), 1030 (sh) cm^{-1}; MS m/e (relative intensity) 238 (2) M^+ (for $C_9H_{10}FeO_4$), 210(7), 182(13), 154(43), 136(7), 126(30), 108(57), 84(38), 56(100).

Reaction of Complex 30 with Acetyl Chloride:

A solution of the anion of complex **30** (827 mg, 3.98 mmol) in ether/HMPA (54 mL:6 mL) was added via double ended needle to a solution of acetyl chloride (0.85 mL, 12 mmol) in ether (5 mL), in a 100 mL R.B. flask fitted with a rubber septum, at -78°C. The reaction was monitored by TLC (silica/toluene) which indicated complete consumption of **30** in 2 hours; then the reaction mixture was poured into brine (250 mL). The layers were separated, and the aqueous layer extracted with ether (3×50 mL). The combined ether extract was washed with saturated sodium hydrogen carbonate (50 mL), then water (50 mL), and dried over $MgSO_4$. The solvent was removed on a rotary evaporator and the crude oil purified by flash chromatography (silica/SkellyB:ether (2:1)) to yield tricarbonyl(4,7,5,6-η-4-methylene-5-hexen-2-one)iron **64** (395 mg, 40%). ^1H nmr (400 MHz, $CDCl_3$) δ5.33 (t, J = 8

Hz, 1H, H5), 3.56 (d, J = 16 Hz, 1H, H3), 3.28 (d, J = 16 Hz, 1H, H3), 2.31 (s, 3H, CH_3), 1.78 (t, J = 2 Hz, 1H, $H7_B$), 1.77 (d of d, J = 7 and 2.5 Hz, 1H, $H6_B$), 0.41 (d, J = 2 Hz, 1H, $H7_A$), 0.22 (d of d, J = 9 and 2.5 Hz, 1H, $H6_A$); IR (CH_2Cl_2 cast) 2050 (s), 1967 (s), 1720 (m) cm^{-1}; MS m/e (relative intensity) 250(13) M^+ (for $C_{10}H_{20}FeO_4$), 222(12), 194(34), 166(100), 56(46).

Reaction of Complex 30 with N,N-Dimethylacetamide:

The anion of complex **30** (543 mg, 2.6 mmol) was prepared as before. N,N-Dimethylacetamide (0.36 mL, 3.9 mmol) was added at -78°C, the mixture warmed to room temperature overnight, then cooled to 0°C and quenched with saturated ammonium chloride (25 mL). The layers were separated and the aqueous layer extracted with Skelly B (3×50 mL). The combined organic extract was successively washed with 1N hydrochloric acid (50 mL), water (50 mL), saturated sodium hydrogen carbonate (50 mL), water (50 mL), and brine (50 mL), then dried over magnesium sulphate, and concentrated (rotary evaporator) to yield tricarbonyl(methyltrimethylenemethane)iron **48** (342 mg, 53%). Yellow oil, bp ca. 50°C (8 torr). ^1H nmr (300 MHz, $CDCl_3$) δ3.01 (d of quartets, J = 6.9 and 2.2 Hz, 1H), 2.48 (d, J = 4.4 Hz, 1H), 2.09 (d, J = 2.2 Hz, 1H), 1.69 (s, 1H), 1.55 (d, J = 4.4 Hz, 1H), 1.28 (d, J = 6.9 Hz, 3H);

^{13}C nmr (75.5 Hz, $CDCl_3$) δ212.08, 211.54, 211.01, 103.99, 73.26, 52.33, 50.28, 15.03; IR (neat film) 2055 (s), 1980 (s) cm^{-1}; MS m/e (relative intensity) 204 (4) M^+ (for $C_8H_8FeO_3$), 180(0.6), 152(2.3), 124(100), 56(67).

Oxidation of Tricarbonyl(diene)iron Complexes (General Procedures), as Illustrated by the Reaction of Complex 51:

Two oxidants were used, trimethylamine oxide and ceric ammonium nitrate.

Method A (Trimethylamine oxide): Complex 51 (398 mg, 1.34 mmol) was dissolved in THF (30 mL), anhydrous trimethylamine oxide (1.052 g, 14.00 mmol) was added, and the slurry heated to 50-55°C (internal temperature). The mixture was kept at this temperature, under argon, for 15 h, then cooled to room temperature and filtered. The filtrate was successively washed with water, then brine, dried over magnesium sulphate, and concentrated (rotary evaporator). The crude oil was purified by flash chromatography (silica/toluene), to yield 3-methylene-5-phenyl-1-pentene **53** (95 mg, 45%). ^1H nmr (400 MHz, $CDCl_3$) δ7.29 (m, 2H), 7.21 (m, 3H), 6.40 (d of d, J = 18 and 11 Hz, 1H), 5.28 (d, J = 18 Hz, 1H), 5.04 (m, J = 11 Hz, 3H), 2.81 (m, 2H), 2.52 (m, 2H); IR ($CHCl_3$ cast) 3080-3020 (m), 2980-2860 (m), 1600 (m), 1500 (m), 990 (m), 897 (s), 745 (m) 698 (s) ~~cm^{-1}; MS~~ m/e (relative intensity) 158(30),

91(100), 65(12); calcd. for $C_{12}H_{14}$ 158.1096, found 158.1098. Anal. Calcd for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 91.07; H, 8.98.

Method B(Ceric Ammonium Nitrate (CAN)): Complex **51** (674 mg, 2.26 mmol) was dissolved in methanol (10 mL), the solution cooled to -16°C, using a 1-octanol/dry-ice cooling bath, and a solution of CAN (2.5 g, 4.6 mmol) in methanol (20 mL) added dropwise with stirring. The progress of the oxidation was monitored by collecting the carbon monoxide evolved in a gas burette. When the addition was complete 73% of the theoretical volume was liberated and so a further two mole equivalents of CAN/MeOH were added. The final volume collected was 95% of the theoretical amount. The cooling bath was removed and the solution warmed to room temperature. The methanol was removed (rotary evaporator) and the residue taken up in water (100 mL). This aqueous solution was extracted with ether (3×50 mL), and the ether washed with brine (50 mL), dried over magnesium sulphate and concentrated (rotary evaporator). The crude oil (310 mg, 87%) was purified by flash chromatography (silica/Skelly B) to yield **53** (143 mg, 40%) identical to that obtained via method A.

Oxidation of Complex 54:

Complex **54** (403 mg, 1.35 mmol) was oxidised using CAN/MeOH as described above. The yield after workup was 160 mg (75%). This pale yellow oil was purified via flash chromatography (silica/Skelly B) to give 8-chloro-3-methylene-1-octene **55** (92 mg, 43%). ^{1}H nmr (400 MHz, $CDCl_3$) δ6.37 (d of d, J = 18 and 11 Hz, 1H), 5.22 (d of d, J = 18 and 0.5 Hz, 1H), 5.06 (d, J = 11 Hz, 1H), 5.03 (brs, 1H), 4.99 (brs, 1H), 3.54 (t, J = 7 Hz, 2H), 2.22 (brt, J = 7 Hz, 2H), 1.80 (quintet, J = 7 Hz, 2H), 1.50 (m, 5H); IR ($CDCl_3$ cast) 2932 (m), 2860 (w), 1633 (s), 855 (m) cm^{-1}; MS m/e (relative intensity) 160(4), 158(8), 109(5). 95(14), 81(16), 68(100), 67(34), 53(14); calcd. for $C_9H_{15}{}^{37}Cl$ 160.0833, found 160.0840, calcd. for $C_9H_{15}{}^{35}Cl$ 158.0862, found 158.0868.

Oxidation of Complex 57:

Complex **57** (175 mg, 0.59 mmol) was oxidised with CAN in the usual manner. The crude oil was purified by column chromatography using silica gel/silver nitrate and eluting with 2% ether:Skelly B. This yielded 3-methylene-1-undecene **58** (78 mg, 80%) as a colourless oil. ^{1}H nmr (400 MHz, $CDCl_3$) δ6.35 (d of d, J = 18 and 11 Hz, 1H), 5.22 (doublet of triplets, J = 18 and 0.5-0.8 Hz, 1H), 5.04 (d of d, J = 11 and 0.8 Hz, 1H), 4.99 (brs, 1H), 4.98 (brs,

1H), 2.20 (t, J = 8 Hz, 2H), 1.48 (brm, 2H), 1.30 (brm, 10H), 0.90 (m, 3H); IR (neat film) 2960 (sh), 2927 (s), 2855 (s), 1640 (m), 1600 (m), 990 (m), 905 (sh), 890 (m) cm^{-1}; MS m/e (relative intensity) 166(46), 139(7), 123(7), 109(21), 98(12), 95(42), 81(60), 68(100), 67(47), 57(43), 53(14); calcd. for $C_{12}H_{22}$ 166.1722, found 166.1721.

Oxidation of Complex 61:

A solution of complex **61** (370 mg, 1.18 mmol) in THF (5 mL) was added to a cooled (-16°C) slurry of CAN (2.64 g, 4.81 mmol) in THF (20 mL). After the addition was complete the cooling bath was removed and the mixture warmed to room temperature. The reaction mixture was filtered, the solid washed with THF and the washings added to the filtrate. The solvent was removed (rotary evaporator), brine (50 mL) was added, and the solution extracted with ether (3×25 mL). The combined extracts were successively washed with water (2×5 mL), then brine (2×5 mL), dried with sodium sulphate and concentrated (rotary evaporator). The crude oil was purified by flash chromatography (silica/40% ether:Skelly B) to yield 3-methylene-5-phenyl-1-penten-5-ol, **62** (68 mg, 33%). ^1H nmr (400 MHz, $CDCl_3$) δ7.32 and 7.24 (d of multiplets, 5H), 6.39 (d of d, J = 18 and 11 Hz, 1H), 5.31 (d, J = 18 Hz, 1H), 5.15 (m, 1H), 5.12 (d, 1H), 5.08 (brs, 1H), 4.82 (d of d, J = 9 and 4 Hz, 1H), 2.70 (d of d, J = 14 and 4 Hz,

1H), 2.56 (d of d, J = 14 and 9 Hz, 1H), 2.06 (brs, 1H); IR ($CHCl_3$ cast) 3420 (m, br), 3080 (m), 306 (sh), 3020 (m), 3000 (sh), 2920 (m), 1630 (w), 1590 (m), 1490 (m), 1450 (m), 1055 (m), 990 (m), 901 (s), 757 (m), 700 (s) cm^{-1}; MS m/e (relative intensity)174(0.8), 156(1.1), 107(100); calcd. for $C_{12}H_{14}O$ 174.1045, found 174.1039. Anal. Calcd for $C_{12}H_{14}$: C, 82.72; H, 8.10. Found: C, 81.95; H, 7.99.

Oxidation of Complex 61 with Trimethylamine Oxide:

Complex **61** (1.10 g, 3.50 mmol) and trimethylamine oxide (3.9 g, 53 mmol) in THF (100 mL) were stirred at room temperature for one hour and then heated to 54°C where it was kept for 3 hours (until gas evolution ceased). The slurry was cooled to room temperature, filtered, and the THF removed (rotary evaporator). The residue was taken up in water (100 mL) and extracted with ether (3×30 mL). The combined ether extracts were successively washed with water (10 mL), then brine (10 mL), dried over magnesium sulphate and concentrated (rotary evaporator) to yield an orange oil (505 mg, 83%). This oil was purified by flash chromatography (silica/30% ether:Skelly B) to yield **62** (105 mg, 17%), identical with that obtained via CAN oxidation.

Reaction of the Isoprene Anion Complex with Water at -78°C and Room Temperature:

The anion complex of **30** was generated by the addition of **30** (64 mg, 3.11 mmol) in 10 mL ether, to a solution of LiTMP (4.4 mL, 4.7 mmol) in 54 mL ether and 6 mL HMPA at -78°C as before. A portion (38 mL) of this solution was removed via double ended needle into a septum-capped measuring cylinder and allowed to warm to room temperature over a period of 2 hours during which time the colour changed from lemon yellow (-78°C) to orange-yellow, to orange-red (room temperature). After reaching room temperature the aliquot was quenched with water (100 mL) and the layers separated. The aqueous layer was extracted with Skelly B (3×50 mL), the combined organic extract washed with 0.1N HCl (25 mL) to remove any TMP, then washed successively with water (25 L), sodium hydrogen carbonate (25 mL) and brine (25 mL), dried over anhydrous magnesium sulphate and concentrated on a rotary evaporator to yield an orange oil (234 mg, 72%). TLC (silica/Skelly B) showed this to be two spots plus some baseline material and this oil was purified by flash chromatography (silica/Skelly B) to yield **48** (104 mg, 32%) as a yellow oil. ^{1}H nmr showed the presence of **30** (8%) in this oil.

The remaining 37 mL of the anion solution at -78°C was quenched with water (100 mL), then warmed to room

temperature and worked up in the same manner as the first aliquot, to yield an orange oil (220 mg, 69%). This oil was purified by flash chromatography (silica/Skelly B) to yield **30** (176 mg, 55%) as a yellow oil.

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